

SEQUENCE LISTING

<110> Lollar, John S.

<120> Nucleic Acid and Amino Acid Sequences
encoding High-Level Expressor Factor VIII Polypeptides and
Methods of Use

<130> 007157/ 276516

<150> PCT/US02/33403

<151> 2002-10-07

<150> 60/327,388

<151> 2001-10-05

<160> 21

<170> FastSEQ for Windows Version 4.0

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<211> 6402

<212> DNA

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<220>

<221> gene

<222> (1)...(6399)

<223> Factor VIII-- Full Length

<221> CDS

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gaa	gac	aac	atc	atg	gta	act	ttc	aaa	aac	cag	gcg	tct	cgt	ccc	tat	4752	
Glu	Asp	Asn	Ile	Met	Val	Thr	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr		
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Ser	Phe	Tyr	Ser	Ser	Leu	Ile	Ser	Tyr	Pro	Asp	Asp	Gln	Glu	Gln	Gly		
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gca	gaa	cct	cga	cac	aac	ttc	gtc	cag	cca	aat	gaa	acc	aga	act	tac	4848	
Ala	Glu	Pro	Arg	His	Asn	Phe	Val	Gln	Pro	Asn	Glu	Thr	Arg	Thr	Tyr		
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Phe	Trp	Lys	Val	Gln	His	His	Met	Ala	Pro	Thr	Glu	Asp	Glu	Phe	Asp		
		1620						1625					1630				
tgc	aaa	gcc	tgg	gcc	tac	ttt	tct	gat	gtt	gac	ctg	gaa	aaa	gat	gtg	4944	
Cys	Lys	Ala	Trp	Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val		
	1635					1640						1645					
cac	tca	ggc	ttg	atc	ggc	ccc	ctt	ctg	atc	tgc	cgc	gcc	aac	acc	ctg	4992	
His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Arg	Ala	Asn	Thr	Leu		
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aac	gct	gct	cac	ggg	aga	caa	gtg	acc	gtg	caa	gaa	ttt	gct	ctg	ttt	5040	
Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe		
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ttc	act	att	ttt	gat	gag	aca	aag	agc	tgg	tac	ttc	act	gaa	aat	gtg	5088	
Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Val		
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Glu	Arg	Asn	Cys	Arg	Ala	Pro	Cys	His	Leu	Gln	Met	Glu	Asp	Pro	Thr		
		1700						1705					1710				

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Leu Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Val Met Asp	
1715 1720 1725	
aca ctc cct ggc tta gta atg gct cag aat caa agg atc cga tgg tat	5232
Thr Leu Pro Gly Leu Val Met Ala Gln Asn Gln Arg Ile Arg Trp Tyr	
1730 1735 1740	
ctg ctc agc atg ggc agc aat gaa aat atc cat tcg att cat ttt agc	5280
Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser	
1745 1750 1755 1760	
gga cac gtg ttc agt gta cgg aaa aag gag gag tat aaa atg gcc gtg	5328
Gly His Val Phe Ser Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Val	
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tac aat ctc tat ccg ggt gtc ttt gag aca gtg gaa atg cta ccg tcc	5376
Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser	
1780 1785 1790	
aaa gtt gga att tgg cga ata gaa tgc ctg att ggc gag cac ctg caa	5424
Lys Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His Leu Gln	
1795 1800 1805	
gct ggg atg agc acg act ttc ctg gtg tac agc aag gag tgt cag gct	5472
Ala Gly Met Ser Thr Thr Phe Leu Val Tyr Ser Lys Glu Cys Gln Ala	
1810 1815 1820	
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Pro Leu Gly Met Ala Ser Gly Arg Ile Arg Asp Phe Gln Ile Thr Ala	
1825 1830 1835 1840	
tca gga cag tat gga cag tgg gcc cca aag ctg gcc aga ctt cat tat	5568
Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr	
1845 1850 1855	
tcc gga tca atc aat gcc tgg agc acc aag gat ccc cac tcc tgg atc	5616
Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro His Ser Trp Ile	
1860 1865 1870	
aag gtg gat ctg ttg gca cca atg atc att cac ggc atc atg acc cag	5664
Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met Thr Gln	
1875 1880 1885	
ggt gcc cgt cag aag ttt tcc agc ctc tac atc tcc cag ttt atc atc	5712
Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile	
1890 1895 1900	
atg tac agt ctt gac ggg agg aac tgg cag agt tac cga ggg aat tcc	5760
Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln Ser Tyr Arg Gly Asn Ser	
1905 1910 1915 1920	
acg ggc acc tta atg gtc ttc ttt ggc aat gtg gac gca tct ggg att	5808
Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ala Ser Gly Ile	
1925 1930 1935	
aaa cac aat att ttt aac cct ccg att gtg gct cgg tac atc cgt ttg	5856
Lys His Asn Ile Phe Asn Pro Pro Ile Val Ala Arg Tyr Ile Arg Leu	
1940 1945 1950	
cac cca aca cat tac agc atc cgc agc act ctt cgc atg gag ttg atg	5904
His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met	
1955 1960 1965	
ggc tgt gat tta aac agt tgc agc atg ccc ctg gga atg cag aat aaa	5952

Gly 1970	Cys	Asp	Leu	Asn	Ser	Cys 1975	Ser	Met	Pro	Leu	Gly 1980	Met	Gln	Asn	Lys	
gcg	ata	tca	gac	tca	cag	atc	acg	gcc	tcc	tcc	cac	cta	agc	aat	ata	6000
Ala	Ile	Ser	Asp	Ser	Gln	Ile	Thr	Ala	Ser	Ser	His	Leu	Ser	Asn	Ile	
1985					1990				1995						2000	
ttt	gcc	acc	tgg	tct	cct	tca	caa	gcc	cga	ctt	cac	ctc	cag	ggg	cgg	6048
Phe	Ala	Thr	Trp	Ser	Pro	Ser	Gln	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	
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acg	aat	gcc	tgg	cga	ccc	cgg	gtg	agc	agc	gca	gag	gag	tgg	ctg	cag	6096
Thr	Asn	Ala	Trp	Arg	Pro	Arg	Val	Ser	Ser	Ala	Glu	Glu	Trp	Leu	Gln	
			2020					2025					2030			
gtg	gac	ctg	cag	aag	acg	gtg	aag	gtc	aca	ggc	atc	acc	acc	cag	ggc	6144
Val	Asp	Leu	Gln	Lys	Thr	Val	Lys	Val	Thr	Gly	Ile	Thr	Thr	Gln	Gly	
		2035				2040						2045				
gtg	aag	tcc	ctg	ctc	agc	agc	atg	tat	gtg	aag	gag	ttc	ctc	gtg	tcc	6192
Val	Lys	Ser	Leu	Leu	Ser	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Val	Ser	
	2050				2055						2060					
agt	agt	cag	gac	ggc	cgc	cgc	tgg	acc	ctg	ttt	ctt	cag	gac	ggc	cac	6240
Ser	Ser	Gln	Asp	Gly	Arg	Arg	Trp	Thr	Leu	Phe	Leu	Gln	Asp	Gly	His	
2065					2070					2075					2080	
acg	aag	gtt	ttt	cag	ggc	aat	cag	gac	tcc	tcc	acc	ccc	gtg	gtg	aac	6288
Thr	Lys	Val	Phe	Gln	Gly	Asn	Gln	Asp	Ser	Ser	Thr	Pro	Val	Val	Asn	
				2085					2090					2095		
gct	ctg	gac	ccc	ccg	ctg	ttc	acg	cgc	tac	ctg	agg	atc	cac	ccc	acg	6336
Ala	Leu	Asp	Pro	Pro	Leu	Phe	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Thr	
			2100					2105					2110			
agc	tgg	gcg	cag	cac	atc	gcc	ctg	agg	ctc	gag	gtt	cta	gga	tgt	gag	6384
Ser	Trp	Ala	Gln	His	Ile	Ala	Leu	Arg	Leu	Glu	Val	Leu	Gly	Cys	Glu	
		2115				2120						2125				
gca	cag	gat	ctc	tac	tga											6402
Ala	Gln	Asp	Leu	Tyr												
		2130														
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Gly	Phe	Ser	Ala	Ile	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
			20					25					30			
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr	
		35					40					45				
Arg	Phe	Pro	Ala	Thr	Ala	Pro	Gly	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val	
		50				55					60					
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser	
65					70				75						80	
Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	
				85					90					95		
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala	
			100					105					110			
Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser	
		115					120						125			

Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu
130						135					140				
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val
145					150				155						160
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr
				165					170					175	
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu
			180					185					190		
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg
	195					200						205			
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu
	210					215						220			
Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met
225					230					235					240
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly
				245					250					255	
Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser
			260					265					270		
Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser
	275					280						285			
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala
	290					295					300				
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu
305					310					315					320
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His
				325					330					335	
His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu
			340					345					350		
Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn
		355					360					365			
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
	370					375					380				
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390					395					400
Trp	Val	His	Tyr	Ile	Ser	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
				405					410					415	
Ala	Val	Pro	Ser	Pro	Ser	Asp	Arg	Ser	Tyr	Lys	Ser	Leu	Tyr	Leu	Asn
			420					425					430		
Ser	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Ala	Arg	Phe	Val
	435					440						445			
Ala	Tyr	Thr	Asp	Val	Thr	Phe	Lys	Thr	Arg	Lys	Ala	Ile	Pro	Tyr	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475						480
Leu	Ile	Ile	Phe	Lys	Asn	Lys	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
				485					490					495	
His	Gly	Ile	Thr	Asp	Val	Ser	Ala	Leu	His	Pro	Gly	Arg	Leu	Leu	Lys
			500					505					510		
Gly	Trp	Lys	His	Leu	Lys	Asp	Met	Pro	Ile	Leu	Pro	Gly	Glu	Thr	Phe
		515				520						525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Ser	Ile	Asn	Leu	Glu	Lys
545					550					555					560
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
				565					570					575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Met	Met	Ser	Asp	Lys	Arg	Asn	Val
			580					585					590		
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Gln	Ser	Trp	Tyr	Leu	Ala	Glu
	595					600						605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Asp	Gly	Leu	Gln	Pro	Gln	Asp
	610					615					620				
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
625					630					635					640
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
				645					650					655	

Tyr	Ile	Leu	Ser	Val	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
			660					665					670		
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
		675					680					685			
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro
		690				695					700				
Gly	Leu	Trp	Val	Leu	Gly	Cys	His	Asn	Ser	Asp	Leu	Arg	Asn	Arg	Gly
705					710					715					720
Met	Thr	Ala	Leu	Leu	Lys	Val	Tyr	Ser	Cys	Asp	Arg	Asp	Ile	Gly	Asp
			725						730					735	
Tyr	Tyr	Asp	Asn	Thr	Tyr	Glu	Asp	Ile	Pro	Gly	Phe	Leu	Leu	Ser	Gly
			740					745					750		
Lys	Asn	Val	Ile	Glu	Pro	Arg	Ser	Phe	Ala	Gln	Asn	Ser	Arg	Pro	Pro
		755					760					765			
Ser	Ala	Ser	Gln	Lys	Gln	Phe	Gln	Thr	Ile	Thr	Ser	Pro	Glu	Asp	Asp
		770				775					780				
Val	Glu	Leu	Asp	Pro	Gln	Ser	Gly	Glu	Arg	Thr	Gln	Ala	Leu	Glu	Glu
785					790					795					800
Leu	Ser	Val	Pro	Ser	Gly	Asp	Gly	Ser	Met	Leu	Leu	Gly	Gln	Asn	Pro
			805						810					815	
Ala	Pro	His	Gly	Ser	Ser	Ser	Ser	Asp	Leu	Gln	Glu	Ala	Arg	Asn	Glu
		820						825					830		
Ala	Asp	Asp	Tyr	Leu	Pro	Gly	Ala	Arg	Glu	Arg	Gly	Thr	Ala	Pro	Ser
		835				840						845			
Ala	Ala	Ala	Arg	Leu	Arg	Pro	Glu	Leu	His	His	Ser	Ala	Glu	Arg	Val
		850				855					860				
Leu	Thr	Pro	Glu	Pro	Glu	Lys	Glu	Leu	Lys	Lys	Leu	Asp	Ser	Lys	Met
865					870					875					880
Ser	Ser	Ser	Ser	Asp	Leu	Leu	Lys	Thr	Ser	Pro	Thr	Ile	Pro	Ser	Asp
			885						890					895	
Thr	Leu	Ser	Ala	Glu	Thr	Glu	Arg	Thr	His	Ser	Leu	Gly	Pro	Pro	His
			900						905				910		
Pro	Gln	Val	Asn	Phe	Arg	Ser	Gln	Leu	Gly	Ala	Ile	Val	Leu	Gly	Lys
		915					920						925		
Asn	Ser	Ser	His	Phe	Ile	Gly	Ala	Gly	Val	Pro	Leu	Gly	Ser	Thr	Glu
		930				935					940				
Glu	Asp	His	Glu	Ser	Ser	Leu	Gly	Glu	Asn	Val	Ser	Pro	Val	Glu	Ser
945					950					955					960
Asp	Gly	Ile	Phe	Glu	Lys	Glu	Arg	Ala	His	Gly	Pro	Ala	Ser	Leu	Thr
			965						970					975	
Lys	Asp	Asp	Val	Leu	Phe	Lys	Val	Asn	Ile	Ser	Leu	Val	Lys	Thr	Asn
		980						985					990		
Lys	Ala	Arg	Val	Tyr	Leu	Lys	Thr	Asn	Arg	Lys	Ile	His	Ile	Asp	Asp
		995					1000					1005			
Ala	Ala	Leu	Leu	Thr	Glu	Asn	Arg	Ala	Ser	Ala	Thr	Phe	Met	Asp	Lys
		1010				1015					1020				
Asn	Thr	Thr	Ala	Ser	Gly	Leu	Asn	His	Val	Ser	Asn	Trp	Ile	Lys	Gly
1025					1030					1035					1040
Pro	Leu	Gly	Lys	Asn	Pro	Leu	Ser	Ser	Glu	Arg	Gly	Pro	Ser	Pro	Glu
			1045						1050					1055	
Leu	Leu	Thr	Ser	Ser	Gly	Ser	Gly	Lys	Ser	Val	Lys	Gly	Gln	Ser	Ser
			1060					1065					1070		
Gly	Gln	Gly	Arg	Ile	Arg	Val	Ala	Val	Glu	Glu	Glu	Glu	Leu	Ser	Lys
		1075				1080						1085			
Gly	Lys	Glu	Met	Met	Leu	Pro	Asn	Ser	Glu	Leu	Thr	Phe	Leu	Thr	Asn
		1090				1095					1100				
Ser	Ala	Asp	Val	Gln	Gly	Asn	Asp	Thr	His	Ser	Gln	Gly	Lys	Lys	Ser
1105					1110					1115					1120
Arg	Glu	Glu	Met	Glu	Arg	Arg	Glu	Lys	Leu	Val	Gln	Glu	Lys	Val	Asp
			1125						1130					1135	
Leu	Pro	Gln	Val	Tyr	Thr	Ala	Thr	Gly	Thr	Lys	Asn	Phe	Leu	Arg	Asn
			1140					1145					1150		
Ile	Phe	His	Gln	Ser	Thr	Glu	Pro	Ser	Val	Glu	Gly	Phe	Asp	Gly	Gly
		1155				1160					1165				
Ser	His	Ala	Pro	Val	Pro	Gln	Asp	Ser	Arg	Ser	Leu	Asn	Asp	Ser	Ala
		1170				1175					1180				

Glu Arg Ala Glu Thr His Ile Ala His Phe Ser Ala Ile Arg Glu Glu	1185	1190	1195	1200
Ala Pro Leu Glu Ala Pro Gly Asn Arg Thr Gly Pro Gly Pro Arg Ser		1205	1210	1215
Ala Val Pro Arg Arg Val Lys Gln Ser Leu Lys Gln Ile Arg Leu Pro		1220	1225	1230
Leu Glu Glu Ile Lys Pro Glu Arg Gly Val Val Leu Asn Ala Thr Ser		1235	1240	1245
Thr Arg Trp Ser Glu Ser Ser Pro Ile Leu Gln Gly Ala Lys Arg Asn		1250	1255	1260
Asn Leu Ser Leu Pro Phe Leu Thr Leu Glu Met Ala Gly Gly Gln Gly		1265	1270	1275
Lys Ile Ser Ala Leu Gly Lys Ser Ala Ala Gly Pro Leu Ala Ser Gly		1285	1290	1295
Lys Leu Glu Lys Ala Val Leu Ser Ser Ala Gly Leu Ser Glu Ala Ser		1300	1305	1310
Gly Lys Ala Glu Phe Leu Pro Lys Val Arg Val His Arg Glu Asp Leu		1315	1320	1325
Leu Pro Gln Lys Thr Ser Asn Val Ser Cys Ala His Gly Asp Leu Gly		1330	1335	1340
Gln Glu Ile Phe Leu Gln Lys Thr Arg Gly Pro Val Asn Leu Asn Lys		1345	1350	1355
Val Asn Arg Pro Gly Arg Thr Pro Ser Lys Leu Leu Gly Pro Pro Met		1365	1370	1375
Pro Lys Glu Trp Glu Ser Leu Glu Lys Ser Pro Lys Ser Thr Ala Leu		1380	1385	1390
Arg Thr Lys Asp Ile Ile Ser Leu Pro Leu Asp Arg His Glu Ser Asn		1395	1400	1405
His Ser Ile Ala Ala Lys Asn Glu Gly Gln Ala Glu Thr Gln Arg Glu		1410	1415	1420
Ala Ala Trp Thr Lys Gln Gly Gly Pro Gly Arg Leu Cys Ala Pro Lys		1425	1430	1435
Pro Pro Val Leu Arg Arg His Gln Arg Asp Ile Ser Leu Pro Thr Phe		1445	1450	1455
Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp Asp Ile Phe Ser Thr Glu		1460	1465	1470
Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly Glu Asp Glu Asn Gln Asp		1475	1480	1485
Pro Arg Ser Phe Gln Lys Arg Thr Arg His Tyr Phe Ile Ala Ala Val		1490	1495	1500
Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu Ser Pro Arg Ala Leu Arg		1505	1510	1515
Asn Arg Ala Gln Asn Gly Glu Val Pro Arg Phe Lys Lys Val Val Phe		1525	1530	1535
Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln Pro Ser Tyr Arg Gly Glu		1540	1545	1550
Leu Asn Lys His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val		1555	1560	1565
Glu Asp Asn Ile Met Val Thr Phe Lys Asn Gln Ala Ser Arg Pro Tyr		1570	1575	1580
Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro Asp Asp Gln Glu Gln Gly		1585	1590	1595
Ala Glu Pro Arg His Asn Phe Val Gln Pro Asn Glu Thr Arg Thr Tyr		1605	1610	1615
Phe Trp Lys Val Gln His His Met Ala Pro Thr Glu Asp Glu Phe Asp		1620	1625	1630
Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val		1635	1640	1645
His Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Arg Ala Asn Thr Leu		1650	1655	1660
Asn Ala Ala His Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe		1665	1670	1675
Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Val		1685	1690	1695
Glu Arg Asn Cys Arg Ala Pro Cys His Leu Gln Met Glu Asp Pro Thr		1700	1705	1710

Leu Lys Glu Asn Tyr Arg Phe His Ala Ile Asn Gly Tyr Val Met Asp
 1715 1720 1725
 Thr Leu Pro Gly Leu Val Met Ala Gln Asn Gln Arg Ile Arg Trp Tyr
 1730 1735 1740
 Leu Leu Ser Met Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser
 1745 1750 1755 1760
 Gly His Val Phe Ser Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Val
 1765 1770 1775
 Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser
 1780 1785 1790
 Lys Val Gly Ile Trp Arg Ile Glu Cys Leu Ile Gly Glu His Leu Gln
 1795 1800 1805
 Ala Gly Met Ser Thr Thr Phe Leu Val Tyr Ser Lys Glu Cys Gln Ala
 1810 1815 1820
 Pro Leu Gly Met Ala Ser Gly Arg Ile Arg Asp Phe Gln Ile Thr Ala
 1825 1830 1835 1840
 Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys Leu Ala Arg Leu His Tyr
 1845 1850 1855
 Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys Asp Pro His Ser Trp Ile
 1860 1865 1870
 Lys Val Asp Leu Leu Ala Pro Met Ile Ile His Gly Ile Met Thr Gln
 1875 1880 1885
 Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile
 1890 1895 1900
 Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln Ser Tyr Arg Gly Asn Ser
 1905 1910 1915 1920
 Thr Gly Thr Leu Met Val Phe Phe Gly Asn Val Asp Ala Ser Gly Ile
 1925 1930 1935
 Lys His Asn Ile Phe Asn Pro Pro Ile Val Ala Arg Tyr Ile Arg Leu
 1940 1945 1950
 His Pro Thr His Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met
 1955 1960 1965
 Gly Cys Asp Leu Asn Ser Cys Ser Met Pro Leu Gly Met Gln Asn Lys
 1970 1975 1980
 Ala Ile Ser Asp Ser Gln Ile Thr Ala Ser Ser His Leu Ser Asn Ile
 1985 1990 1995 2000
 Phe Ala Thr Trp Ser Pro Ser Gln Ala Arg Leu His Leu Gln Gly Arg
 2005 2010 2015
 Thr Asn Ala Trp Arg Pro Arg Val Ser Ser Ala Glu Glu Trp Leu Gln
 2020 2025 2030
 Val Asp Leu Gln Lys Thr Val Lys Val Thr Gly Ile Thr Thr Gln Gly
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 Val Lys Ser Leu Leu Ser Ser Met Tyr Val Lys Glu Phe Leu Val Ser
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 Ser Ser Gln Asp Gly Arg Arg Trp Thr Leu Phe Leu Gln Asp Gly His
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 Ala Leu Asp Pro Pro Leu Phe Thr Arg Tyr Leu Arg Ile His Pro Thr
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Gly	Phe	Ser	Ala	Ile	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
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tgg	gac	tac	cgg	caa	agt	gaa	ctc	ctc	cgt	gag	ctg	cac	gtg	gac	acc	144
Trp	Asp	Tyr	Arg	Gln	Ser	Glu	Leu	Leu	Arg	Glu	Leu	His	Val	Asp	Thr	
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aga	ttt	cct	gct	aca	gcg	cca	gga	gct	ctt	ccg	ttg	ggc	ccg	tca	gtc	192
Arg	Phe	Pro	Ala	Thr	Ala	Pro	Gly	Ala	Leu	Pro	Leu	Gly	Pro	Ser	Val	
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ctg	tac	aaa	aag	act	gtg	ttc	gta	gag	ttc	acg	gat	caa	ctt	ttc	agc	240
Leu	Tyr	Lys	Lys	Thr	Val	Phe	Val	Glu	Phe	Thr	Asp	Gln	Leu	Phe	Ser	
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Val	Ala	Arg	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	
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cag	gct	gag	gtt	tac	gac	acg	gtg	gtc	gtt	acc	ctg	aag	aac	atg	gct	336
Gln	Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Val	Thr	Leu	Lys	Asn	Met	Ala	
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Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser	
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Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu	
	130					135					140					
gac	gat	aaa	gtc	ctt	ccc	ggg	aaa	agc	caa	acc	tac	gtc	tgg	cag	gtc	480
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val	
145					150				155					160		
ctg	aaa	gaa	aat	ggg	cca	aca	gcc	tct	gac	cca	cca	tgt	ctt	acc	tac	528
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr	
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tca	tac	ctg	tct	cac	gtg	gac	ctg	gtg	aaa	gac	ctg	aat	tcg	ggc	ctc	576
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	
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Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg	
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acc	cag	aac	ctg	cac	gaa	ttt	gta	cta	ctt	ttt	gct	gtc	ttt	gat	gaa	672
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	
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Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met	
225					230				235					240		
gat	ccc	gca	cct	gcc	agg	gcc	cag	cct	gca	atg	cac	aca	gtc	aat	ggc	768
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly	

245										250										255										
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Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser															
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Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser															
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att	ttt	ctt	gaa	ggc	cac	acg	ttt	ctc	gtg	agg	cac	cat	cgc	cag	gct	912														
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala															
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Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu															
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Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His															
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His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu															
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ccc	cag	ctg	cgg	agg	aaa	gct	gat	gaa	gag	gaa	gat	tat	gat	gac	aat	1104														
Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn															
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Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val															
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tct	ccc	ttt	atc	caa	atc	cgc	tcg	gtt	gcc	aag	aag	cat	ccc	aaa	acc	1200														
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr															
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tgg	gtg	cac	tac	atc	tct	gca	gag	gag	gag	gac	tgg	gac	tac	gcc	ccc	1248														
Trp	Val	His	Tyr	Ile	Ser	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro															
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gcg	gtc	ccc	agc	ccc	agt	gac	aga	agt	tat	aaa	agt	ctc	tac	ttg	aac	1296														
Ala	Val	Pro	Ser	Pro	Ser	Asp	Arg	Ser	Tyr	Lys	Ser	Leu	Tyr	Leu	Asn															
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agt	ggt	cct	cag	cga	att	ggt	agg	aaa	tac	aaa	aaa	gct	cga	ttc	gtc	1344														
Ser	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Ala	Arg	Phe	Val															
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gct	tac	acg	gat	gta	aca	ttt	aag	act	cgt	aaa	gct	att	ccg	tat	gaa	1392														
Ala	Tyr	Thr	Asp	Val	Thr	Phe	Lys	Thr	Arg	Lys	Ala	Ile	Pro	Tyr	Glu															
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Leu	Ile	Ile	Phe	Lys	Asn	Lys	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro															
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cat	gga	atc	act	gat	gtc	agc	gct	ttg	cac	cca	ggg	aga	ctt	cta	aaa	1536														
His	Gly	Ile	Thr	Asp	Val	Ser	Ala	Leu	His	Pro	Gly	Arg	Leu	Leu	Lys															
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ggt tgg aaa cat ttg aaa gac atg cca att ctg cca gga gag act ttc	1584
Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe	
515 520 525	
aag tat aaa tgg aca gtg act gtg gaa gat ggg cca acc aag tcc gat	1632
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
530 535 540	
cct cgg tgc ctg acc cgc tac tac tcg agc tcc att aat cta gag aaa	1680
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ser Ile Asn Leu Glu Lys	
545 550 555 560	
gat ctg gct tcg gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa	1728
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
tct gta gac caa aga gga aac cag atg atg tca gac aag aga aac gtc	1776
Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val	
580 585 590	
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Ile Leu Phe Ser Val Phe Asp Glu Asn Gln Ser Trp Tyr Leu Ala Glu	
595 600 605	
aat att cag cgc ttc ctc ccc aat ccg gat gga tta cag ccc cag gat	1872
Asn Ile Gln Arg Phe Leu Pro Asn Pro Asp Gly Leu Gln Pro Gln Asp	
610 615 620	
cca gag ttc caa gct tct aac atc atg cac agc atc aat ggc tat gtt	1920
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
625 630 635 640	
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp	
645 650 655	
tac att cta agt gtt gga gca cag acg gac ttc ctc tcc gtc ttc ttc	2016
Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe	
660 665 670	
tct ggc tac acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc	2064
Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr	
675 680 685	
ctg ttc ccc ttc tca gga gaa acg gtc ttc atg tca atg gaa aac cca	2112
Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro	
690 695 700	
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Gly Leu Trp Val Leu Gly Cys His Asn Ser Asp Leu Arg Asn Arg Gly	
705 710 715 720	
atg aca gcc tta ctg aag gtg tat agt tgt gac agg gac att ggt gat	2208
Met Thr Ala Leu Leu Lys Val Tyr Ser Cys Asp Arg Asp Ile Gly Asp	
725 730 735	
tat tat gac aac act tat gaa gat att cca ggc ttc ttg ctg agt gga	2256
Tyr Tyr Asp Asn Thr Tyr Glu Asp Ile Pro Gly Phe Leu Leu Ser Gly	
740 745 750	
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Lys Asn Val Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro	
755 760 765	
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Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp	

770	775	780	
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cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro 915 920 925	2784		
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro 930 935 940	2832		
aat gaa acc aga act tac ttt tgg aaa gtg cag cat cac atg gca ccc Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro 945 950 955 960	2880		
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val 965 970 975	2928		
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Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile	
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Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr	
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Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu	
1125 1130 1135	
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Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr	
1140 1145 1150	
agc aag gag tgt cag gct cca ctg gga atg gct tct gga cgc att aga	3504
Ser Lys Glu Cys Gln Ala Pro Leu Gly Met Ala Ser Gly Arg Ile Arg	
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Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys	
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ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag	3600
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys	
1185 1190 1195 1200	
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Asp Pro His Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile	
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Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Arg Asn Trp Gln	
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1250 1255 1260	
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Val Asp Ala Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Val	
1265 1270 1275 1280	
gct cgg tac atc cgt ttg cac cca aca cat tac agc atc cgc agc act	3888
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr	
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 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
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 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
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Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu		175
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Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu		205
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Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu		300
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Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val		365
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Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu		445
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp		640
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Tyr Ile Leu Ser Val Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe		655

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Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu	Asn	Ser	Cys	Ser	Met	Pro
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Gly	Ile	Thr	Thr	Gln	Gly	Val	Lys	Ser	Leu	Leu	Ser	Ser	Met	Tyr	Val
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Lys	Glu	Phe	Leu	Val	Ser	Ser	Ser	Gln	Asp	Gly	Arg	Arg	Trp	Thr	Leu
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 ctgtgccttt tgcgattctg ctttagt gcc acc aga aga tac tac ctg ggt gca 234
 Ala Thr Arg Arg Tyr Tyr Leu Gly Ala

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 Val Glu Leu Ser Trp Asp Tyr Met Gln Ser Asp Leu Gly Glu Leu Pro
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 Val Asp Ala Arg Phe Pro Pro Arg Val Pro Lys Ser Phe Pro Phe Asn
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Thr Ser Val Val Tyr Lys Lys Thr Leu Phe Val Glu Phe Thr Val His	
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Leu Phe Asn Ile Ala Lys Pro Arg Pro Pro Trp Met Gly Leu Leu Gly	
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Pro Thr Ile Gln Ala Glu Val Tyr Asp Thr Val Val Ile Thr Leu Lys	
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Asn Met Ala Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Tyr	
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Gly Ala Tyr Ala Pro Val Leu Gln Asp Phe Arg Ser Leu Asn Asp Ser	
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Thr Asn Arg Thr Lys Lys His Thr Ala His Phe Ser Lys Lys Gly Glu	
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Lys Tyr Ala Cys Thr Thr Arg Ile Ser Pro Asn Thr Ser Gln Gln Asn	
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Phe Val Thr Gln Arg Ser Lys Arg Ala Leu Lys Gln Phe Arg Leu Pro	
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Leu Glu Glu Thr Glu Leu Glu Lys Arg Ile Ile Val Asp Asp Thr Ser	
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Thr Gln Trp Ser Lys Asn Met Lys His Leu Thr Pro Ser Thr Leu Thr	
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Gln Ile Asp Tyr Asn Glu Lys Glu Lys Gly Ala Ile Thr Gln Ser Pro	

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tct cca tta ccc att gca aag gta tca tca ttt cca tct att aga cct Ser Pro Leu Pro Ile Ala Lys Val Ser Ser Phe Pro Ser Ile Arg Pro 1390 1395 1400			4410
ata tat ctg acc agg gtc cta ttc caa gac aac tct tct cat ctt cca Ile Tyr Leu Thr Arg Val Leu Phe Gln Asp Asn Ser Ser His Leu Pro 1405 1410 1415			4458
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gcc aca aat tca gtc aca tac aag aaa gtt gag aac act gtt ctc ccg Ala Thr Asn Ser Val Thr Tyr Lys Lys Val Glu Asn Thr Val Leu Pro 1470 1475 1480			4650
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tct cct ggc cat ctg gat ctc gtg gaa ggg agc ctt ctt cag gga aca Ser Pro Gly His Leu Asp Leu Val Glu Gly Ser Leu Leu Gln Gly Thr 1515 1520 1525			4794
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Trp Ala Lys Gln Gly Arg Thr Glu Arg Leu Cys Ser Gln Asn Pro Pro	
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Val Leu Lys Arg His Gln Arg Glu Ile Thr Arg Thr Thr Leu Gln Ser	
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Asp Gln Glu Glu Ile Asp Tyr Asp Asp Thr Ile Ser Val Glu Met Lys	
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Lys Glu Asp Phe Asp Ile Tyr Asp Glu Asp Glu Asn Gln Ser Pro Arg	
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Ser Phe Gln Lys Lys Thr Arg His Tyr Phe Ile Ala Ala Val Glu Arg	
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Ala Gln Ser Gly Ser Val Pro Gln Phe Lys Lys Val Val Phe Gln Glu	
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Glu His Leu Gly Leu Leu Gly Pro Tyr Ile Arg Ala Glu Val Glu Asp	
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Tyr Ser Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu	
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Pro Arg Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp	
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Lys Val Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys	
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Asn	Cys	Arg	Ala	Pro	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	
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Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile	Asn	Gly	Tyr	Ile	Met	Asp	Thr	Leu	
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Pro	Gly	Leu	Val	Met	Ala	Gln	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	
1930					1935					1940					1945	
agc	atg	ggc	agc	aat	gaa	aac	atc	cat	tct	att	cat	ttc	agt	gga	cat	6090
Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile	His	Ser	Ile	His	Phe	Ser	Gly	His	
1950					1955					1960						
gtg	ttc	act	gta	cga	aaa	aaa	gag	gag	tat	aaa	atg	gca	ctg	tac	aat	6138
Val	Phe	Thr	Val	Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Leu	Tyr	Asn	
1965					1970					1975						
ctc	tat	cca	ggg	gtt	ttt	gag	aca	gtg	gaa	atg	tta	cca	tcc	aaa	gct	6186
Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr	Val	Glu	Met	Leu	Pro	Ser	Lys	Ala	
1980					1985					1990						
gga	att	tgg	cgg	gtg	gaa	tgc	ctt	att	ggc	gag	cat	cta	cat	gct	ggg	6234
Gly	Ile	Trp	Arg	Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	His	Ala	Gly	
1995					2000					2005						
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Met	Ser	Thr	Leu	Phe	Leu	Val	Tyr	Ser	Asn	Lys	Cys	Gln	Thr	Pro	Leu	
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Gly	Met	Ala	Ser	Gly	His	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	
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Gln	Tyr	Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	
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Ser	Ile	Asn	Ala	Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	
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Asp	Leu	Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	
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Arg	Gln	Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	
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agt	ctt	gat	ggg	aag	aag	tgg	cag	act	tat	cga	gga	aat	tcc	act	gga	6570
Ser	Leu	Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	
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acc	tta	atg	gtc	ttc	ttt	ggc	aat	gtg	gat	tca	tct	ggg	ata	aaa	cac	6618
Thr	Leu	Met	Val	Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	
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Asn	Ile	Phe	Asn	Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	
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Ser Asp Ala Gln Ile Thr Ala Ser Ser Tyr Phe Thr Asn Met Phe Ala	
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Gln Asp Gly His Gln Trp Thr Leu Phe Phe Gln Asn Gly Lys Val Lys	
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Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile Gln Ala Glu Val
65     70     75     80
Tyr Asp Thr Val Val Ile Thr Leu Lys Asn Met Ala Ser His Pro Val
85     90     95
Ser Leu His Ala Val Gly Val Ser Tyr Trp Lys Ala Ser Glu Gly Ala
100    105    110
Glu Tyr Asp Asp Gln Thr Ser Gln Arg Glu Lys Glu Asp Asp Lys Val
115    120    125
Phe Pro Gly Gly Ser His Thr Tyr Val Trp Gln Val Leu Lys Glu Asn
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Gly Pro Met Ala Ser Asp Pro Leu Cys Leu Thr Tyr Ser Tyr Leu Ser
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His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu Ile Gly Ala Leu
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Leu Val Cys Arg Glu Gly Ser Leu Ala Lys Glu Lys Thr Gln Thr Leu
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His Lys Phe Ile Leu Leu Phe Ala Val Phe Asp Glu Gly Lys Ser Trp
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His Ser Glu Thr Lys Asn Ser Leu Met Gln Asp Arg Asp Ala Ala Ser
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Ala Arg Ala Trp Pro Lys Met His Thr Val Asn Gly Tyr Val Asn Arg
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Ser Leu Pro Gly Leu Ile Gly Cys His Arg Lys Ser Val Tyr Trp His
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Val Ile Gly Met Gly Thr Thr Pro Glu Val His Ser Ile Phe Leu Glu
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Gly His Thr Phe Leu Val Arg Asn His Arg Gln Ala Ser Leu Glu Ile
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Ser Pro Ile Thr Phe Leu Thr Ala Gln Thr Leu Leu Met Asp Leu Gly
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Gln Phe Leu Leu Phe Cys His Ile Ser Ser His Gln His Asp Gly Met
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Glu Ala Tyr Val Lys Val Asp Ser Cys Pro Glu Glu Pro Gln Leu Arg
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Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr Trp Val His

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Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu Leu Ile Ile				
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Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro His Gly Ile				
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His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe Lys Tyr Lys				
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34

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Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	Tyr	Pro	Lys	Thr
385					390					395					400
Trp	Ile	His	Tyr	Ile	Ser	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
			405						410					415	
Ser	Val	Pro	Thr	Ser	Asp	Asn	Gly	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Ser
		420						425					430		
Asn	Gly	Pro	His	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Ile
	435					440						445			
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Thr	Ile	Gln	His	Glu
	450					455					460				
Ser	Gly	Leu	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475						480
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
			485						490				495		
His	Gly	Ile	Thr	Asp	Val	Ser	Pro	Leu	His	Ala	Arg	Arg	Leu	Pro	Arg
		500						505					510		
Gly	Ile	Lys	His	Val	Lys	Asp	Leu	Pro	Ile	His	Pro	Gly	Glu	Ile	Phe
	515						520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Ile	Asn	Pro	Glu	Arg
545					550				555						560
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
			565						570					575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Met	Met	Ser	Asp	Lys	Arg	Asn	Val
		580						585					590		
Ile	Leu	Phe	Ser	Ile	Phe	Asp	Glu	Asn	Gln	Ser	Trp	Tyr	Ile	Thr	Glu
	595						600					605			
Asn	Met	Gln	Arg	Phe	Leu	Pro	Asn	Ala	Ala	Lys	Thr	Gln	Pro	Gln	Asp
	610					615						620			

Pro	Gly	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
625					630					635					640
Phe	Asp	Ser	Leu	Glu	Leu	Thr	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
			645						650						655
His	Ile	Leu	Ser	Val	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Ile	Phe	Phe
			660						665						670
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
		675						680					685		
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro
		690						695				700			
Gly	Leu	Trp	Val	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Lys	Arg	Gly
705					710					715					720
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Ser	Thr	Ser	Asp
					725					730					735
Tyr	Tyr	Glu	Glu	Ile	Tyr	Glu	Asp	Ile	Pro	Thr	Gln	Leu	Val	Asn	Glu
			740						745						750
Asn	Asn	Val	Ile	Asp	Pro	Arg	Ser	Phe	Phe	Gln	Asn	Thr	Asn	His	Pro
		755													765
Asn	Thr	Arg	Lys	Lys	Lys	Phe	Lys	Asp	Ser	Thr	Ile	Pro	Lys	Asn	Asp
		770						775							780
Met	Glu	Lys	Ile	Glu	Pro	Gln	Phe	Glu	Glu	Ile	Ala	Glu	Met	Leu	Lys
785						790					795				800
Val	Gln	Ser	Val	Ser	Val	Ser	Asp	Met	Leu	Met	Leu	Leu	Gly	Gln	Ser
					805					810					815
His	Pro	Thr	Pro	His	Gly	Leu	Phe	Leu	Ser	Asp	Gly	Gln	Glu	Ala	Ile
			820							825					830
Tyr	Glu	Ala	Ile	His	Asp	Asp	His	Ser	Pro	Asn	Ala	Ile	Asp	Ser	Asn
		835													845
Glu	Gly	Pro	Ser	Lys	Val	Thr	Gln	Leu	Arg	Pro	Glu	Ser	His	His	Ser
		850													860
Glu	Lys	Ile	Val	Phe	Thr	Pro	Gln	Pro	Gly	Leu	Gln	Leu	Arg	Ser	Asn
865						870					875				880
Lys	Ser	Leu	Glu	Thr	Thr	Ile	Glu	Val	Lys	Trp	Lys	Lys	Leu	Gly	Leu
					885					890					895
Gln	Val	Ser	Ser	Leu	Pro	Ser	Asn	Leu	Met	Thr	Thr	Thr	Ile	Leu	Ser
					900					905					910
Asp	Asn	Leu	Lys	Ala	Thr	Phe	Glu	Lys	Thr	Asp	Ser	Ser	Gly	Phe	Pro
		915													925
Asp	Met	Pro	Val	His	Ser	Ser	Ser	Lys	Leu	Ser	Thr	Thr	Ala	Phe	Gly
		930													940
Lys	Lys	Ala	Tyr	Ser	Leu	Val	Gly	Ser	His	Val	Pro	Leu	Asn	Ala	Ser
945						950					955				960
Glu	Glu	Asn	Ser	Asp	Ser	Asn	Ile	Leu	Asp	Ser	Thr	Leu	Met	Tyr	Ser
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Gln	Glu	Ser	Leu	Pro	Arg	Asp	Asn	Ile	Leu	Ser	Ile	Glu	Asn	Asp	Arg
					980										990
Leu	Leu	Arg	Glu	Lys	Arg	Phe	His	Gly	Ile	Ala	Leu	Leu	Thr	Lys	Asp
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Asn	Thr	Leu	Phe	Lys	Asp	Asn	Val	Ser	Leu	Met	Lys	Thr	Asn	Lys	Thr
					1010										1020
Tyr	Asn	His	Ser	Thr	Thr	Asn	Glu	Lys	Leu	His	Thr	Glu	Ser	Pro	Thr
1025						1030					1035				1040
Ser	Ile	Glu	Asn	Ser	Thr	Thr	Asp	Leu	Gln	Asp	Ala	Ile	Leu	Lys	Val
					1045						1050				1055
Asn	Ser	Glu	Ile	Gln	Glu	Val	Thr	Ala	Leu	Ile	His	Asp	Gly	Thr	Leu
					1060										1070
Leu	Gly	Lys	Asn	Ser	Thr	Tyr	Leu	Arg	Leu	Asn	His	Met	Leu	Asn	Arg
					1075										1085
Thr	Thr	Ser	Thr	Lys	Asn	Lys	Asp	Ile	Phe	His	Arg	Lys	Asp	Glu	Asp
					1090										1100
Pro	Ile	Pro	Gln	Asp	Glu	Glu	Asn	Thr	Ile	Met	Pro	Phe	Ser	Lys	Met
1105						1110					1115				1120
Leu	Phe	Leu	Ser	Glu	Ser	Ser	Asn	Trp	Phe	Lys	Lys	Thr	Asn	Gly	Asn
					1125										1135
Asn	Ser	Leu	Asn	Ser	Glu	Gln	Glu	His	Ser	Pro	Lys	Gln	Leu	Val	Tyr
					1140										1150

Leu Met Phe Lys Lys Tyr Val Lys Asn Gln Ser Phe Leu Ser Glu Lys
 1155 1160 1165
 Asn Lys Val Thr Val Glu Gln Asp Gly Phe Thr Lys Asn Ile Gly Leu
 1170 1175 1180
 Lys Asp Met Ala Phe Pro His Asn Met Ser Ile Phe Leu Thr Thr Leu
 1185 1190 1195 1200
 Ser Asn Val His Glu Asn Gly Arg His Asn Gln Glu Lys Asn Ile Gln
 1205 1210 1215
 Glu Glu Ile Glu Lys Glu Ala Leu Ile Glu Glu Lys Val Val Leu Pro
 1220 1225 1230
 Gln Val His Glu Ala Thr Gly Ser Lys Asn Phe Leu Lys Asp Ile Leu
 1235 1240 1245
 Ile Leu Gly Thr Arg Gln Asn Ile Ser Leu Tyr Glu Val His Val Pro
 1250 1255 1260
 Val Leu Gln Asn Ile Thr Ser Ile Asn Asn Ser Thr Asn Thr Val Gln
 1265 1270 1275 1280
 Ile His Met Glu His Phe Phe Lys Arg Arg Lys Asp Lys Glu Thr Asn
 1285 1290 1295
 Ser Glu Gly Leu Val Asn Lys Thr Arg Glu Met Val Lys Asn Tyr Pro
 1300 1305 1310
 Ser Gln Lys Asn Ile Thr Thr Gln Arg Ser Lys Arg Ala Leu Gly Gln
 1315 1320 1325
 Phe Arg Leu Ser Thr Gln Trp Leu Lys Thr Ile Asn Cys Ser Thr Gln
 1330 1335 1340
 Cys Ile Ile Lys Gln Ile Asp His Ser Lys Glu Met Lys Lys Phe Ile
 1345 1350 1355 1360
 Thr Lys Ser Ser Leu Ser Asp Ser Ser Val Ile Lys Ser Thr Thr Gln
 1365 1370 1375
 Thr Asn Ser Ser Asp Ser His Ile Val Lys Thr Ser Ala Phe Pro Pro
 1380 1385 1390
 Ile Asp Leu Lys Arg Ser Pro Phe Gln Asn Lys Phe Ser His Val Gln
 1395 1400 1405
 Ala Ser Ser Tyr Ile Tyr Asp Phe Lys Thr Lys Ser Ser Arg Ile Gln
 1410 1415 1420
 Glu Ser Asn Asn Phe Leu Lys Glu Thr Lys Ile Asn Asn Pro Ser Leu
 1425 1430 1435 1440
 Ala Ile Leu Pro Trp Asn Met Phe Ile Asp Gln Gly Lys Phe Thr Ser
 1445 1450 1455
 Pro Gly Lys Ser Asn Thr Asn Ser Val Thr Tyr Lys Lys Arg Glu Asn
 1460 1465 1470
 Ile Ile Phe Leu Lys Pro Thr Leu Pro Glu Glu Ser Gly Lys Ile Glu
 1475 1480 1485
 Leu Leu Pro Gln Val Ser Ile Gln Glu Glu Glu Ile Leu Pro Thr Glu
 1490 1495 1500
 Thr Ser His Gly Ser Pro Gly His Leu Asn Leu Met Lys Glu Val Phe
 1505 1510 1515 1520
 Leu Gln Lys Ile Gln Gly Pro Thr Lys Trp Asn Lys Ala Lys Arg His
 1525 1530 1535
 Gly Glu Ser Ile Lys Gly Lys Thr Glu Ser Ser Lys Asn Thr Arg Ser
 1540 1545 1550
 Lys Leu Leu Asn His His Ala Trp Asp Tyr His Tyr Ala Ala Gln Ile
 1555 1560 1565
 Pro Lys Asp Met Trp Lys Ser Lys Glu Lys Ser Pro Glu Ile Ile Ser
 1570 1575 1580
 Ile Lys Gln Glu Asp Thr Ile Leu Ser Leu Arg Pro His Gly Asn Ser
 1585 1590 1595 1600
 His Ser Ile Gly Ala Asn Glu Lys Gln Asn Trp Pro Gln Arg Glu Thr
 1605 1610 1615
 Thr Trp Val Lys Gln Gly Gln Thr Gln Arg Thr Cys Ser Gln Ile Pro
 1620 1625 1630
 Pro Val Leu Lys Arg His Gln Arg Glu Leu Ser Ala Phe Gln Ser Glu
 1635 1640 1645
 Gln Glu Ala Thr Asp Tyr Asp Asp Ala Ile Thr Ile Glu Thr Ile Glu
 1650 1655 1660
 Asp Phe Asp Ile Tyr Ser Glu Asp Ile Lys Gln Gly Pro Arg Ser Phe
 1665 1670 1675 1680

Gln	Gln	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp	1685	1690	1695
Asp	Tyr	Gly	Met	Ser	Thr	Ser	His	Val	Leu	Arg	Asn	Arg	Tyr	Gln	Ser	1700	1705	1710
Asp	Asn	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr	Asp	1715	1720	1725
Gly	Ser	Phe	Ser	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His	Leu	1730	1735	1740
Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	Met	1745	1750	1755
Val	Thr	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	1765	1770	1775
Leu	Ile	Ser	Tyr	Lys	Glu	Asp	Gln	Arg	Gly	Glu	Glu	Pro	Arg	Arg	Asn	1780	1785	1790
Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Ile	Tyr	Phe	Trp	Lys	Val	Gln	His	1795	1800	1805
His	Met	Ala	Pro	Thr	Glu	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	Ala	Tyr	1810	1815	1820
Phe	Ser	Asp	Val	Asp	Leu	Glu	Arg	Asp	Met	His	Ser	Gly	Leu	Ile	Gly	1825	1830	1835
Pro	Leu	Leu	Ile	Cys	His	Ala	Asn	Thr	Leu	Asn	Pro	Ala	His	Gly	Arg	1845	1850	1855
Gln	Val	Ser	Val	Gln	Glu	Phe	Ala	Leu	Leu	Phe	Thr	Ile	Phe	Asp	Glu	1860	1865	1870
Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Val	Lys	Arg	Asn	Cys	Lys	Thr	1875	1880	1885
Pro	Cys	Asn	Phe	Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	1890	1895	1900
Phe	His	Ala	Ile	Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	1905	1910	1915
Met	Ala	Gln	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Asn	1925	1930	1935
Asn	Glu	Asn	Ile	Gln	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Thr	Val	1940	1945	1950
Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	1955	1960	1965
Val	Phe	Glu	Thr	Leu	Glu	Met	Ile	Pro	Ser	Arg	Ala	Gly	Ile	Trp	Arg	1970	1975	1980
Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Leu	1985	1990	1995
Phe	Leu	Val	Tyr	Ser	Lys	Gln	Cys	Gln	Ile	Pro	Leu	Gly	Met	Ala	Ser	2005	2010	2015
Gly	Ser	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	His	Tyr	Gly	Gln	2020	2025	2030
Trp	Ala	Pro	Asn	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	Asn	Ala	2035	2040	2045
Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	Leu	Ala	2050	2055	2060
Pro	Met	Ile	Val	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	Lys	Phe	2065	2070	2075
Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu	Asp	Gly	2085	2090	2095
Lys	Lys	Trp	Leu	Ser	Tyr	Gln	Gly	Asn	Ser	Thr	Gly	Thr	Leu	Met	Val	2100	2105	2110
Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	Asn	Ser	Phe	Asn	2115	2120	2125
Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	Thr	His	Ser	Ser	2130	2135	2140
Ile	Arg	Ser	Thr	Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu	Asn	Ser	2145	2150	2155
Cys	Ser	Ile	Pro	Leu	Gly	Met	Glu	Ser	Lys	Val	Ile	Ser	Asp	Thr	Gln	2165	2170	2175
Ile	Thr	Ala	Ser	Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp	Ser	Pro	2180	2185	2190
Ser	Gln	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Thr	Asn	Ala	Trp	Arg	Pro	2195	2200	2205

Gln Val Asn Asp Pro Lys Gln Trp Leu Gln Val Asp Leu Gln Lys Thr
 2210 2215 2220
 Met Lys Val Thr Gly Ile Ile Thr Gln Gly Val Lys Ser Leu Phe Thr
 2225 2230 2235 2240
 Ser Met Phe Val Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His
 2245 2250 2255
 His Trp Thr Gln Ile Leu Tyr Asn Gly Lys Val Lys Val Phe Gln Gly
 2260 2265 2270
 Asn Gln Asp Ser Ser Thr Pro Met Met Asn Ser Leu Asp Pro Pro Leu
 2275 2280 2285
 Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ile Trp Glu His Gln Ile
 2290 2295 2300
 Ala Leu Arg Leu Glu Ile Leu Gly Cys Glu Ala Gln Gln Gln Tyr
 2305 2310 2315

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 <211> 14
 <212> PRT
 <213> Homo sapeins

<220>
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 <222> (1)...(14)
 <223> Linker sequence

<400> 9
 Ser Phe Ser Gln Asn Pro Pro Val Leu Lys Arg His Gln Arg
 1 5 10

<210> 10
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 <212> PRT
 <213> Homo sapiens

<400> 10
 Arg His Gln Arg
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<210> 11
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 <212> PRT
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<220>
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 <222> (1)...(24)
 <223> Linker sequence

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 Ser Phe Ala Gln Asn Ser Arg Pro Pro Ser Ala Ser Ala Pro Lys Pro
 1 5 10 15
 Pro Val Leu Arg Arg His Gln Arg
 20

<210> 12
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 <212> DNA
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<223> B domain-deleted factor VIII
(HSQ)

<400> 12

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Met	Gln	Ile	Glu	Leu	Ser	Thr	Cys	Phe	Phe	Leu	Cys	Leu	Leu	Arg	Phe	
1				5					10					15		
tgc	ttt	agt	gcc	acc	aga	aga	tac	tac	ctg	ggc	gca	gtg	gaa	ctg	tca	96
Cys	Phe	Ser	Ala	Thr	Arg	Arg	Tyr	Tyr	Leu	Gly	Ala	Val	Glu	Leu	Ser	
			20					25					30			
tgg	gac	tat	atg	caa	agt	gat	ctc	ggc	gag	ctg	cct	gtg	gac	gca	aga	144
Trp	Asp	Tyr	Met	Gln	Ser	Asp	Leu	Gly	Glu	Leu	Pro	Val	Asp	Ala	Arg	
		35					40					45				
ttt	cct	cct	aga	gtg	cca	aaa	tct	ttt	cca	ttc	aac	acc	tca	gtc	gtg	192
Phe	Pro	Pro	Arg	Val	Pro	Lys	Ser	Phe	Pro	Phe	Asn	Thr	Ser	Val	Val	
	50					55					60					
tac	aaa	aag	act	ctg	ttt	gta	gaa	ttc	acg	ggt	cac	ctt	ttc	aac	atc	240
Tyr	Lys	Lys	Thr	Leu	Phe	Val	Glu	Phe	Thr	Val	His	Leu	Phe	Asn	Ile	
	65				70				75						80	
gct	aag	cca	agg	cca	ccc	tgg	atg	ggc	ctg	cta	ggc	cct	acc	atc	cag	288
Ala	Lys	Pro	Arg	Pro	Pro	Trp	Met	Gly	Leu	Leu	Gly	Pro	Thr	Ile	Gln	
				85					90					95		
gct	gag	ggt	tat	gat	aca	gtg	gtc	att	aca	ctt	aag	aac	atg	gct	tcc	336
Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Ile	Thr	Leu	Lys	Asn	Met	Ala	Ser	
			100					105					110			
cat	cct	gtc	agt	ctt	cat	gct	ggt	gta	tcc	tac	tgg	aaa	gct	tct		384
His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Tyr	Trp	Lys	Ala	Ser	
		115					120				125					
gag	gga	gct	gaa	tat	gat	gat	cag	acc	agt	caa	agg	gag	aaa	gaa	gat	432
Glu	Gly	Ala	Glu	Tyr	Asp	Asp	Gln	Thr	Ser	Gln	Arg	Glu	Lys	Glu	Asp	
	130					135					140					
gat	aaa	gtc	ttc	cct	ggc	gga	agc	cat	aca	tat	gtc	tgg	cag	gtc	ctg	480
Asp	Lys	Val	Phe	Pro	Gly	Gly	Ser	His	Thr	Tyr	Val	Trp	Gln	Val	Leu	
	145				150					155					160	
aaa	gag	aat	ggc	cca	atg	gcc	tct	gac	cca	ctg	tgc	ctt	acc	tac	tca	528
Lys	Glu	Asn	Gly	Pro	Met	Ala	Ser	Asp	Pro	Leu	Cys	Leu	Thr	Tyr	Ser	
			165					170						175		
tat	ctt	tct	cat	gtg	gac	ctg	gta	aaa	gac	ttg	aat	tca	ggc	ctc	att	576
Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	Ile	
			180					185					190			
gga	gcc	cta	cta	gta	tgt	aga	gaa	ggg	agt	ctg	gcc	aag	gaa	aag	aca	624
Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Ala	Lys	Glu	Lys	Thr	
		195					200					205				
cag	acc	ttg	cac	aaa	ttt	ata	cta	ctt	ttt	gct	gta	ttt	gat	gaa	ggg	672
Gln	Thr	Leu	His	Lys	Phe	Ile	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	Gly	
	210					215					220					
aaa	agt	tgg	cac	tca	gaa	aca	aag	aac	tcc	ttg	atg	cag	gat	agg	gat	720
Lys	Ser	Trp	His	Ser	Glu	Thr	Lys	Asn	Ser	Leu	Met	Gln	Asp	Arg	Asp	
	225				230					235				240		
gct	gca	tct	gct	cgg	gcc	tgg	cct	aaa	atg	cac	aca	gtc	aat	ggc	tat	768

Ala	Ala	Ser	Ala	Arg	Ala	Trp	Pro	Lys	Met	His	Thr	Val	Asn	Gly	Tyr		
				245					250					255			
gta	aac	agg	tct	ctg	cca	ggg	ctg	att	gga	tgc	cac	agg	aaa	tca	gtc	816	
Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Arg	Lys	Ser	Val		
			260					265					270				
tat	tgg	cat	gtg	att	gga	atg	ggc	acc	act	cct	gaa	gtg	cac	tca	ata	864	
Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Thr	Pro	Glu	Val	His	Ser	Ile		
			275				280					285					
ttc	ctc	gaa	ggg	cac	aca	ttt	ctt	gtg	agg	aac	cat	cgc	cag	gcg	tcc	912	
Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	Asn	His	Arg	Gln	Ala	Ser		
		290					295				300						
ttg	gaa	atc	tcg	cca	ata	act	ttc	ctt	act	gct	caa	aca	ctc	ttg	atg	960	
Leu	Glu	Ile	Ser	Pro	Ile	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Leu	Leu	Met		
	305					310				315					320		
gac	ctt	gga	cag	ttt	cta	ctg	ttt	tgt	cat	atc	tct	tcc	cac	caa	cat	1008	
Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	Gln	His		
				325					330					335			
gat	ggc	atg	gaa	gct	tat	gtc	aaa	gta	gac	agc	tgt	cca	gag	gaa	ccc	1056	
Asp	Gly	Met	Glu	Ala	Tyr	Val	Lys	Val	Asp	Ser	Cys	Pro	Glu	Glu	Pro		
			340					345					350				
caa	cta	cga	atg	aaa	aat	aat	gaa	gaa	gcg	gaa	gac	tat	gat	gat	gat	1104	
Gln	Leu	Arg	Met	Lys	Asn	Asn	Glu	Glu	Ala	Glu	Asp	Tyr	Asp	Asp	Asp		
		355					360					365					
ctt	act	gat	tct	gaa	atg	gat	gtg	gtc	agg	ttt	gat	gat	gac	aac	tct	1152	
Leu	Thr	Asp	Ser	Glu	Met	Asp	Val	Val	Arg	Phe	Asp	Asp	Asp	Asn	Ser		
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Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro		
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tta	gtc	ctc	gcc	ccc	gat	gac	aga	agt	tat	aaa	agt	caa	tat	ttg	aac	1296	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn		
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aat	ggc	cct	cag	cgg	att	ggg	agg	aag	tac	aaa	aaa	gtc	cga	ttt	atg	1344	
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met		
			435				440					445					
gca	tac	aca	gat	gaa	acc	ttt	aag	acg	cgt	gaa	gct	att	cag	cat	gaa	1392	
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu		
			450				455				460						
tca	gga	atc	ttg	gga	cct	tta	ctt	tat	ggg	gaa	gtt	gga	gac	aca	ctg	1440	
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu		
					470					475					480		
ttg	att	ata	ttt	aag	aat	caa	gca	agc	aga	cca	tat	aac	atc	tac	cct	1488	
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro		
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His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys		
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Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe	
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
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Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg	
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Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
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Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val	
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Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu	
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Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp	
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Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
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Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp	
645 650 655	
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Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe	
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Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr	
675 680 685	
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Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro	
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Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly	
705 710 715 720	
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Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp	
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Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys	
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Asn Asn Ala Ile Glu Pro Arg Ser Phe Ser Gln Asn Pro Pro Val Leu	
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Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu		
785					790				795						800		
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Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp		
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Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln		
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Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser		
			900					905					910				
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Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg		
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aaa	aac	ttt	gtc	aag	cct	aat	gaa	acc	aaa	act	tac	ttt	tgg	aaa	gtg	2832	
Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val		
	930					935					940						
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Gln	His	His	Met	Ala	Pro	Thr	Lys	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp		
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Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu		
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Ile	Gly	Pro	Leu	Leu	Val	Cys	His	Thr	Asn	Thr	Leu	Asn	Pro	Ala	His		
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	1025				1030					1035					1040		

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Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly	
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Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met	
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Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe	
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Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr	
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cca ggt gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att	3360
Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile	
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Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser	
1125 1130 1135	
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Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met	
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Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu	
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Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln	
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Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu	
1220 1225 1230	
gat ggg aag aag tgg cag act tat cga gga aat tcc act gga acc tta	3744
Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu	
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Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile	
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Tyr																	

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Tyr	Lys	Lys	Thr	Leu	Phe	Val	Glu	Phe	Thr	Val	His	Leu	Phe	Asn	Ile	
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Ala	Glu	Val	Tyr	Asp	Thr	Val	Val	Ile	Thr	Leu	Lys	Asn	Met	Ala	Ser	
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His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Tyr	Trp	Lys	Ala	Ser	
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Glu	Gly	Ala	Glu	Tyr	Asp	Asp	Gln	Thr	Ser	Gln	Arg	Glu	Lys	Glu	Asp
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Asp	Lys	Val	Phe	Pro	Gly	Gly	Ser	His	Thr	Tyr	Val	Trp	Gln	Val	Leu
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Lys	Glu	Asn	Gly	Pro	Met	Ala	Ser	Asp	Pro	Leu	Cys	Leu	Thr	Tyr	Ser
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Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu	Ile
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Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Ala	Lys	Glu	Lys	Thr
	195						200					205			
Gln	Thr	Leu	His	Lys	Phe	Ile	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu	Gly
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Lys	Ser	Trp	His	Ser	Glu	Thr	Lys	Asn	Ser	Leu	Met	Gln	Asp	Arg	Asp
225					230					235					240
Ala	Ala	Ser	Ala	Arg	Ala	Trp	Pro	Lys	Met	His	Thr	Val	Asn	Gly	Tyr
				245					250					255	
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	275						280					285			
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	290					295					300				
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Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	Gln	His
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Pro	Ser	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
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Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
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His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
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Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
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Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
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Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
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Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly
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Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp
			725						730					735	
Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys
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Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu
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Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln
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Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu
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Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe
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Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp
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Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr
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Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His
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Leu	Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile
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Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser
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Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg
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Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val
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Gln	His	His	Met	Ala	Pro	Thr	Lys	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp
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Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu
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Asn Ala Trp Ser Thr Lys Glu Pro Phe Ser Trp Ile Lys Val Asp Leu
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 Leu Ala Pro Met Ile Ile His Gly Ile Lys Thr Gln Gly Ala Arg Gln
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 Lys Phe Ser Ser Leu Tyr Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu
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 Asp Gly Lys Lys Trp Gln Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu
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 Met Val Phe Phe Gly Asn Val Asp Ser Ser Gly Ile Lys His Asn Ile
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 Phe Asn Pro Pro Ile Ile Ala Arg Tyr Ile Arg Leu His Pro Thr His
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 Tyr Ser Ile Arg Ser Thr Leu Arg Met Glu Leu Met Gly Cys Asp Leu
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 Ser Pro Ser Lys Ala Arg Leu His Leu Gln Gly Arg Ser Asn Ala Trp
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 Lys Thr Met Lys Val Thr Gly Val Thr Thr Gln Gly Val Lys Ser Leu
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 Gln Gly Asn Gln Asp Ser Phe Thr Pro Val Val Asn Ser Leu Asp Pro
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 Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His
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 Tyr

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 <212> DNA
 <213> Artificial Sequence

<220>
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<221> CDS
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 domains: Alp-A2p-app-A3p-C1h-C2h

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 ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val

50	55	60	
ctg tac aaa aag act	gtg ttc gta gag ttc	acg gat caa ctt ttc agc	240
Leu Tyr Lys Lys Thr	Val Phe Val Glu Phe Thr	Asp Gln Leu Phe Ser	
65	70	75 80	
ggt gcc agg ccc agg	cca cca tgg atg ggt	ctg ctg ggt cct acc atc	288
Val Ala Arg Pro Arg	Pro Pro Trp Met Gly	Leu Leu Gly Pro Thr Ile	
	85	90 95	
cag gct gag gtt tac	gac acg gtg gtc gtt	acc ctg aag aac atg gct	336
Gln Ala Glu Val Tyr	Asp Thr Val Val Thr	Leu Lys Asn Met Ala	
	100	105 110	
tct cat ccc gtt agt	ctt cac gct gtc ggc	gtc tcc ttc tgg aaa tct	384
Ser His Pro Val Ser	Leu His Ala Val Gly	Val Ser Phe Trp Lys Ser	
	115	120 125	
tcc gaa ggc gct gaa	tat gag gat cac acc	agc caa agg gag aag gaa	432
Ser Glu Gly Ala Glu	Tyr Glu Asp His Thr	Ser Gln Arg Glu Lys Glu	
	130	135 140	
gac gat aaa gtc ctt	ccc ggt aaa agc caa	acc tac gtc tgg cag gtc	480
Asp Asp Lys Val Leu	Pro Gly Lys Ser Gln	Thr Tyr Val Trp Gln Val	
	145	150 155 160	
ctg aaa gaa aat ggt	cca aca gcc tct gac	cca cca tgt ctt acc tac	528
Leu Lys Glu Asn Gly	Pro Thr Ala Ser Asp	Pro Pro Cys Leu Thr Tyr	
	165	170 175	
tca tac ctg tct cac	gtg gac ctg gtg aaa	gac ctg aat tcg ggc ctc	576
Ser Tyr Leu Ser His	Val Asp Leu Val Lys	Asp Leu Asn Ser Gly Leu	
	180	185 190	
att gga gcc ctg ctg	gtt tgt aga gaa ggg	agt ctg acc aga gaa agg	624
Ile Gly Ala Leu Leu	Val Cys Arg Glu Gly	Ser Leu Thr Arg Glu Arg	
	195	200 205	
acc cag aac ctg cac	gaa ttt gta cta ctt	ttt gct gtc ttt gat gaa	672
Thr Gln Asn Leu His	Glu Phe Val Leu Leu	Phe Ala Val Phe Asp Glu	
	210	215 220	
ggg aaa agt tgg cac	tca gca aga aat gac	tcc tgg aca cgg gcc atg	720
Gly Lys Ser Trp His	Ser Ala Arg Asn Asp	Ser Trp Thr Arg Ala Met	
	225	230 235 240	
gat ccc gca cct gcc	agg gcc cag cct gca	atg cac aca gtc aat ggc	768
Asp Pro Ala Pro Ala	Arg Ala Gln Pro Ala	Met His Thr Val Asn Gly	
	245	250 255	
tat gtc aac agg tct	ctg cca ggt ctg atc	gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser	Leu Pro Gly Leu Ile	Gly Cys His Lys Lys Ser	
	260	265 270	
gtc tac tgg cac gtg	att gga atg ggc acc	agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val	Ile Gly Met Gly Thr	Ser Pro Glu Val His Ser	
	275	280 285	
att ttt ctt gaa ggc	cac acg ttt ctc gtg	agg cac cat cgc cag gct	912
Ile Phe Leu Glu Gly	His Thr Phe Leu Val	Arg His His Arg Gln Ala	
	290	295 300	
tcc ttg gag atc tcg	cca cta act ttc ctc	act gct cag aca ttc ctg	960
Ser Leu Glu Ile Ser	Pro Leu Thr Phe Leu	Thr Ala Gln Thr Phe Leu	
	305	310 315 320	

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Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
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His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
340 345 350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn	
355 360 365	
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Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tcg gtt gcc aag aag cat ccc aaa acc	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tgg gtg cac tac atc tct gca gag gag gag gac tgg gac tac gcc ccc	1248
Trp Val His Tyr Ile Ser Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
gcg gtc ccc agc ccc agt gac aga agt tat aaa agt ctc tac ttg aac	1296
Ala Val Pro Ser Pro Ser Asp Arg Ser Tyr Lys Ser Leu Tyr Leu Asn	
420 425 430	
agt ggt cct cag cga att ggt agg aaa tac aaa aaa gct cga ttc gtc	1344
Ser Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Ala Arg Phe Val	
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gct tac acg gat gta aca ttt aag act cgt aaa gct att ccg tat gaa	1392
Ala Tyr Thr Asp Val Thr Phe Lys Thr Arg Lys Ala Ile Pro Tyr Glu	
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Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
465 470 475 480	
ttg att ata ttt aag aat aaa gcg agc cga cca tat aac atc tac cct	1488
Leu Ile Ile Phe Lys Asn Lys Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
485 490 495	
cat gga atc act gat gtc agc gct ttg cac cca ggg aga ctt cta aaa	1536
His Gly Ile Thr Asp Val Ser Ala Leu His Pro Gly Arg Leu Leu Lys	
500 505 510	
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Gly Trp Lys His Leu Lys Asp Met Pro Ile Leu Pro Gly Glu Thr Phe	
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Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
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Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Ile Asn Leu Glu Lys	
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Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
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Ser Val Asp Gln Arg Gly Asn Gln Met Met Ser Asp Lys Arg Asn Val	

580										585										590										
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Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Gln	Ser	Trp	Tyr	Leu	Ala	Glu															
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aat	att	cag	cgc	ttc	ctc	ccc	aat	ccg	gat	gga	tta	cag	ccc	cag	gat	1872														
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Asp	Gly	Leu	Gln	Pro	Gln	Asp															
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cca	gag	ttc	caa	gct	tct	aac	atc	atg	cac	agc	atc	aat	ggc	tat	gtt	1920														
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Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp															
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Tyr	Ile	Leu	Ser	Val	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe															
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Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro															
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705					710					715					720															
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Met	Thr	Ala	Leu	Leu	Lys	Val	Tyr	Ser	Cys	Asp	Arg	Asp	Ile	Gly	Asp															
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740					745					750																				
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755					760					765																				
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Ser	Ala	Ser	Ala	Pro	Lys	Pro	Pro	Val	Leu	Arg	Arg	His	Gln	Arg	Asp															
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785					790					795					800															
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Ser	Pro	Arg	Ala	Leu	Arg	Asn	Arg	Ala	Gln	Asn	Gly	Glu	Val	Pro	Arg	
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Pro	Ser	Tyr	Arg	Gly	Glu	Leu	Asn	Lys	His	Leu	Gly	Leu	Leu	Gly	Pro	
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Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val	
		995					1000					1005				
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Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp	
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Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile	
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	1090					1095					1100					
gag	tat	aaa	atg	gcc	gtg	tac	aat	ctc	tat	ccg	ggc	gtc	ttt	gag	aca	3360
Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr	

1105	1110	1115	1120	
gtg gaa atg cta ccg tcc aaa gtt gga att tgg cga ata gaa tgc ctg				3408
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu	1125	1130	1135	
att ggc gag cac ctg caa gct ggg atg agc acg act ttc ctg gtg tac				3456
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr	1140	1145	1150	
agc aag aag tgt cag act ccc ctg gga atg gct tct gga cac att aga				3504
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg	1155	1160	1165	
gat ttt cag att aca gct tca gga caa tat gga cag tgg gcc cca aag				3552
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys	1170	1175	1180	
ctg gcc aga ctt cat tat tcc gga tca atc aat gcc tgg agc acc aag				3600
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys	1185	1190	1195	1200
gag ccc ttt tct tgg atc aag gtg gat ctg ttg gca cca atg att att				3648
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile	1205	1210	1215	
cac ggc atc aag acc cag ggt gcc cgt cag aag ttc tcc agc ctc tac				3696
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr	1220	1225	1230	
atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag				3744
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln	1235	1240	1245	
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat				3792
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn	1250	1255	1260	
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att				3840
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile	1265	1270	1275	1280
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act				3888
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr	1285	1290	1295	
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca				3936
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro	1300	1305	1310	
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca				3984
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser	1315	1320	1325	
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga				4032
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg	1330	1335	1340	
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat				4080
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn	1345	1350	1355	1360
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca				4128
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr	1365	1370	1375	

gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg 4176
 Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val
 1380 1385 1390
 aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc 4224
 Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu
 1395 1400 1405
 ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc 4272
 Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser
 1410 1415 1420
 ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac 4320
 Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr
 1425 1430 1435 1440
 ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg 4368
 Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met
 1445 1450 1455
 gag gtt ctg ggc tgc gag gca cag gac ctc tac 4401
 Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
 1460 1465

<210> 15
 <211> 1467
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> HP44/OL-- factor VIII having the following
 domains: Alp-A2p-app-A3p-Clh-C2h

<400> 15
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
 1 5 10 15
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly

59

770		775		780
Ile Ser Leu Pro Thr Phe	Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp			
785		790		800
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly		795		
		805		815
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His		810		
		820		830
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu		825		
		835		845
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg		840		
		850		860
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln		855		
		865		875
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro		870		880
		885		895
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn		890		
		900		910
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro		905		
		915		925
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro		920		
		930		940
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro		935		
		945		955
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val		950		960
		965		975
Asp Leu Glu Lys Asp Val His Ser Gly Leu Ile Gly Pro Leu Leu Ile		970		
		980		990
Cys Arg Ala Asn Thr Leu Asn Ala Ala His Gly Arg Gln Val Thr Val		985		
		995		1005
Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe Asp Glu Thr Lys Ser Trp		1000		
		1010		1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu		1015		
		1025		1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile		1030		1040
		1045		1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn		1050		
		1060		1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile		1065		
		1075		1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu		1080		
		1090		1100
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr		1095		
		1105		1115
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu		1110		1120
		1125		1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr		1130		
		1140		1150
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg		1145		
		1155		1165
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys		1160		
		1170		1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys		1175		
		1185		1195
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile		1190		1200
		1205		1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr		1210		
		1220		1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln		1225		
		1235		1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn		1240		
		1250		1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile		1255		
		1265		1275
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr		1270		1280
		1285		1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro		1290		

1300	1305	1310
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser		
1315	1320	1325
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg		
1330	1335	1340
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn		
1345	1350	1355
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr		
1365	1370	1375
Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val		
1380	1385	1390
Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu		
1395	1400	1405
Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser		
1410	1415	1420
Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr		
1425	1430	1435
Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met		
1445	1450	1455
Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr		
1460	1465	

<210> 16

<211> 4371

<212> DNA

<213> Artificial Sequence

<220>

<223> hybrid human and porcine factor VIII sequence

<221> CDS

<222> (1)...(4371)

<223> HP46/SQ-- factor VIII having the following domains: Alp-A2h-aph-A3h-C1h-C2h

<400> 16

atg cag cta gag ctc tcc acc tgt gtc ttt ctg tgt ctc ttg cca ctc	48
Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu	
1 5 10 15	
ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc	96
Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser	
20 25 30	
tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc	144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr	
35 40 45	
aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc	192
Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val	
50 55 60	
ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc	240
Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser	
65 70 75 80	
gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc	288
Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile	
85 90 95	
cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct	336
Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala	
100 105 110	
tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct	384

Ser	His	Pro	Val	Ser	Leu	His	Ala	Val	Gly	Val	Ser	Phe	Trp	Lys	Ser		
		115					120					125					
tcc	gaa	ggc	gct	gaa	tat	gag	gat	cac	acc	agc	caa	agg	gag	aag	gaa	432	
Ser	Glu	Gly	Ala	Glu	Tyr	Glu	Asp	His	Thr	Ser	Gln	Arg	Glu	Lys	Glu		
	130					135					140						
gac	gat	aaa	gtc	ctt	ccc	ggg	aaa	agc	caa	acc	tac	gtc	tgg	cag	gtc	480	
Asp	Asp	Lys	Val	Leu	Pro	Gly	Lys	Ser	Gln	Thr	Tyr	Val	Trp	Gln	Val		
	145				150					155					160		
ctg	aaa	gaa	aat	ggg	cca	aca	gcc	tct	gac	cca	cca	tgt	ctt	acc	tac	528	
Leu	Lys	Glu	Asn	Gly	Pro	Thr	Ala	Ser	Asp	Pro	Pro	Cys	Leu	Thr	Tyr		
				165					170					175			
tca	tac	ctg	tct	cac	gtg	gac	ctg	gtg	aaa	gac	ctg	aat	tgc	ggc	ctc	576	
Ser	Tyr	Leu	Ser	His	Val	Asp	Leu	Val	Lys	Asp	Leu	Asn	Ser	Gly	Leu		
				180				185					190				
att	gga	gcc	ctg	ctg	gtt	tgt	aga	gaa	ggg	agt	ctg	acc	aga	gaa	agg	624	
Ile	Gly	Ala	Leu	Leu	Val	Cys	Arg	Glu	Gly	Ser	Leu	Thr	Arg	Glu	Arg		
		195				200						205					
acc	cag	aac	ctg	cac	gaa	ttt	gta	cta	ctt	ttt	gct	gtc	ttt	gat	gaa	672	
Thr	Gln	Asn	Leu	His	Glu	Phe	Val	Leu	Leu	Phe	Ala	Val	Phe	Asp	Glu		
	210					215					220						
ggg	aaa	agt	tgg	cac	tca	gca	aga	aat	gac	tcc	tgg	aca	cgg	gcc	atg	720	
Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met		
	225				230					235					240		
gat	ccc	gca	cct	gcc	agg	gcc	cag	cct	gca	atg	cac	aca	gtc	aat	ggc	768	
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly		
				245					250					255			
tat	gtc	aac	agg	tct	ctg	cca	ggg	ctg	atc	gga	tgt	cat	aag	aaa	tca	816	
Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser		
			260					265					270				
gtc	tac	tgg	cac	gtg	att	gga	atg	ggc	acc	agc	ccg	gaa	gtg	cac	tcc	864	
Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser		
		275					280					285					
att	ttt	ctt	gaa	ggc	cac	acg	ttt	ctc	gtg	agg	cac	cat	cgc	cag	gct	912	
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala		
	290					295					300						
tcc	ttg	gag	atc	tgc	cca	cta	act	ttc	ctc	act	gct	cag	aca	ttc	ctg	960	
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu		
	305				310					315					320		
atg	gac	ctt	ggc	cag	ttc	cta	ctg	ttt	tgt	cat	atc	tct	tcc	cac	cac	1008	
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His		
				325					330					335			
cat	ggg	ggc	atg	gag	gct	cac	gtc	aga	gta	gaa	agc	tgc	gcc	gag	gag	1056	
His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu		
			340					345					350				
ccc	cag	ctg	cgg	agg	aaa	gct	gat	gaa	gag	gaa	gat	tat	gat	gac	aat	1104	
Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn		
		355					360					365					
ttg	tac	gac	tgc	gac	atg	gac	gtg	gtc	cgg	ctc	gat	ggg	gac	gac	gtg	1152	
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val		
		370				375					380						

tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tggtta gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc	1248
Trp Val His Tyr Ile Ala Ala Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac	1296
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg	1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met	
435 440 445	
gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa	1392
Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu	
450 455 460	
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg	1440
Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu	
465 470 475 480	
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct	1488
Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro	
485 490 495	
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa	1536
His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys	
500 505 510	
gggtta gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc	1584
Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe	
515 520 525	
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat	1632
Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp	
530 535 540	
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga	1680
Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg	
545 550 555 560	
gat cta gct tca gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa	1728
Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu	
565 570 575	
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc	1776
Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val	
580 585 590	
atc ctgttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag	1824
Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu	
595 600 605	
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat	1872
Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp	
610 615 620	
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt	1920
Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val	
625 630 635 640	
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg	1968

Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp		
				645					650					655			
tac	att	cta	agc	att	gga	gca	cag	act	gac	ttc	ctt	tct	gtc	ttc	ttc	2016	
Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe		
			660					665					670				
tct	gga	tat	acc	ttc	aaa	cac	aaa	atg	gtc	tat	gaa	gac	aca	ctc	acc	2064	
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr		
			675				680					685					
cta	ttc	cca	ttc	tca	gga	gaa	act	gtc	ttc	atg	tcg	atg	gaa	aac	cca	2112	
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro		
			690				695					700					
ggg	cta	tgg	att	ctg	ggg	tgc	cac	aac	tca	gac	ttt	cgg	aac	aga	ggc	2160	
Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly		
					710					715					720		
atg	acc	gcc	tta	ctg	aag	gtt	tct	agt	tgt	gac	aag	aac	act	ggg	gat	2208	
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp		
				725				730						735			
tat	tac	gag	gac	agt	tat	gaa	gat	att	tca	gca	tac	ttg	ctg	agt	aaa	2256	
Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys		
			740					745					750				
aac	aat	gcc	att	gaa	cct	agg	agc	ttc	tct	cag	aat	cca	cca	gtc	ttg	2304	
Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu		
			755				760					765					
aaa	cgc	cat	caa	cgg	gaa	ata	act	cgt	act	act	ctt	cag	tca	gat	caa	2352	
Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln		
			770				775					780					
gag	gaa	att	gac	tat	gat	gat	acc	ata	tca	gtt	gaa	atg	aag	aag	gaa	2400	
Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu		
					790					795					800		
gat	ttt	gac	att	tat	gat	gag	gat	gaa	aat	cag	agc	ccc	cgc	agc	ttt	2448	
Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe		
				805					810					815			
caa	aag	aaa	aca	cga	cac	tat	ttt	att	gct	gca	gtg	gag	agg	ctc	tgg	2496	
Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp		
			820					825					830				
gat	tat	ggg	atg	agt	agc	tcc	cca	cat	gtt	cta	aga	aac	agg	gct	cag	2544	
Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln		
			835				840						845				
agt	ggc	agt	gtc	cct	cag	ttc	aag	aaa	gtt	gtt	ttc	cag	gaa	ttt	act	2592	
Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr		
			850				855					860					
gat	ggc	tcc	ttt	act	cag	ccc	tta	tac	cgt	gga	gaa	cta	aat	gaa	cat	2640	
Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His		
					870					875					880		
ttg	gga	ctc	ctg	ggg	cca	tat	ata	aga	gca	gaa	gtt	gaa	gat	aat	atc	2688	
Leu	Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile		
				885					890						895		
atg	gta	act	ttc	aga	aat	cag	gcc	tct	cgt	ccc	tat	tcc	ttc	tat	tct	2736	
Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser		
			900					905							910		

agc ctt att tct tat gag gaa gat cag agg caa gga gca gaa cct aga	2784
Ser Leu Ile Ser Tyr Glu Glu Asp Gln Arg Gln Gly Ala Glu Pro Arg	
915 920 925	
aaa aac ttt gtc aag cct aat gaa acc aaa act tac ttt tgg aaa gtg	2832
Lys Asn Phe Val Lys Pro Asn Glu Thr Lys Thr Tyr Phe Trp Lys Val	
930 935 940	
caa cat cat atg gca ccc act aaa gat gag ttt gac tgc aaa gcc tgg	2880
Gln His His Met Ala Pro Thr Lys Asp Glu Phe Asp Cys Lys Ala Trp	
945 950 955 960	
gct tat ttc tct gat gtt gac ctg gaa aaa gat gtg cac tca ggc ctg	2928
Ala Tyr Phe Ser Asp Val Asp Leu Glu Lys Asp Val His Ser Gly Leu	
965 970 975	
att gga ccc ctt ctg gtc tgc cac act aac aca ctg aac cct gct cat	2976
Ile Gly Pro Leu Leu Val Cys His Thr Asn Thr Leu Asn Pro Ala His	
980 985 990	
ggg aga caa gtg aca gta cag gaa ttt gct ctg ttt ttc acc atc ttt	3024
Gly Arg Gln Val Thr Val Gln Glu Phe Ala Leu Phe Phe Thr Ile Phe	
995 1000 1005	
gat gag acc aaa agc tgg tac ttc act gaa aat atg gaa aga aac tgc	3072
Asp Glu Thr Lys Ser Trp Tyr Phe Thr Glu Asn Met Glu Arg Asn Cys	
1010 1015 1020	
agg gct ccc tgc aat atc cag atg gaa gat ccc act ttt aaa gag aat	3120
Arg Ala Pro Cys Asn Ile Gln Met Glu Asp Pro Thr Phe Lys Glu Asn	
1025 1030 1035 1040	
tat cgc ttc cat gca atc aat ggc tac ata atg gat aca cta cct ggc	3168
Tyr Arg Phe His Ala Ile Asn Gly Tyr Ile Met Asp Thr Leu Pro Gly	
1045 1050 1055	
tta gta atg gct cag gat caa agg att cga tgg tat ctg ctc agc atg	3216
Leu Val Met Ala Gln Asp Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met	
1060 1065 1070	
ggc agc aat gaa aac atc cat tct att cat ttc agt gga cat gtg ttc	3264
Gly Ser Asn Glu Asn Ile His Ser Ile His Phe Ser Gly His Val Phe	
1075 1080 1085	
act gta cga aaa aaa gag gag tat aaa atg gca ctg tac aat ctc tat	3312
Thr Val Arg Lys Lys Glu Glu Tyr Lys Met Ala Leu Tyr Asn Leu Tyr	
1090 1095 1100	
cca ggt gtt ttt gag aca gtg gaa atg tta cca tcc aaa gct gga att	3360
Pro Gly Val Phe Glu Thr Val Glu Met Leu Pro Ser Lys Ala Gly Ile	
1105 1110 1115 1120	
tgg cgg gtg gaa tgc ctt att ggc gag cat cta cat gct ggg atg agc	3408
Trp Arg Val Glu Cys Leu Ile Gly Glu His Leu His Ala Gly Met Ser	
1125 1130 1135	
aca ctt ttt ctg gtg tac agc aat aag tgt cag act ccc ctg gga atg	3456
Thr Leu Phe Leu Val Tyr Ser Asn Lys Cys Gln Thr Pro Leu Gly Met	
1140 1145 1150	
gct tct gga cac att aga gat ttt cag att aca gct tca gga caa tat	3504
Ala Ser Gly His Ile Arg Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr	
1155 1160 1165	
gga cag tgg gcc cca aag ctg gcc aga ctt cat tat tcc gga tca atc	3552

Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile		
1170						1175					1180						
aat	gcc	tgg	agc	acc	aag	gag	ccc	ttt	tct	tgg	atc	aag	gtg	gat	ctg	3600	
Asn	Ala	Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu		
1185					1190					1195					1200		
ttg	gca	cca	atg	att	att	cac	ggc	atc	aag	acc	cag	ggg	gcc	cgt	cag	3648	
Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln		
				1205						1210					1215		
aag	ttc	tcc	agc	ctc	tac	atc	tct	cag	ttt	atc	atc	atg	tat	agt	ctt	3696	
Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu		
			1220					1225					1230				
gat	ggg	aag	aag	tgg	cag	act	tat	cga	gga	aat	tcc	act	gga	acc	tta	3744	
Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	Thr	Leu		
		1235					1240					1245					
atg	gtc	ttc	ttt	ggc	aat	gtg	gat	tca	tct	ggg	ata	aaa	cac	aat	att	3792	
Met	Val	Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	Asn	Ile		
	1250					1255					1260						
ttt	aac	cct	cca	att	att	gct	cga	tac	atc	cgt	ttg	cac	cca	act	cat	3840	
Phe	Asn	Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	Thr	His		
1265					1270					1275					1280		
tat	agc	att	cgc	agc	act	ctt	cgc	atg	gag	ttg	atg	ggc	tgt	gat	tta	3888	
Tyr	Ser	Ile	Arg	Ser	Thr	Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu		
				1285					1290					1295			
aat	agt	tgc	agc	atg	cca	ttg	gga	atg	gag	agt	aaa	gca	ata	tca	gat	3936	
Asn	Ser	Cys	Ser	Met	Pro	Leu	Gly	Met	Glu	Ser	Lys	Ala	Ile	Ser	Asp		
			1300					1305					1310				
gca	cag	att	act	gct	tca	tcc	tac	ttt	acc	aat	atg	ttt	gcc	acc	tgg	3984	
Ala	Gln	Ile	Thr	Ala	Ser	Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp		
		1315					1320					1325					
tct	cct	tca	aaa	gct	cga	ctt	cac	ctc	caa	ggg	agg	agt	aat	gcc	tgg	4032	
Ser	Pro	Ser	Lys	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Ser	Asn	Ala	Trp		
	1330					1335					1340						
aga	cct	cag	gtg	aat	aat	cca	aaa	gag	tgg	ctg	caa	gtg	gac	ttc	cag	4080	
Arg	Pro	Gln	Val	Asn	Asn	Pro	Lys	Glu	Trp	Leu	Gln	Val	Asp	Phe	Gln		
1345					1350					1355					1360		
aag	aca	atg	aaa	gtc	aca	gga	gta	act	act	cag	gga	gta	aaa	tct	ctg	4128	
Lys	Thr	Met	Lys	Val	Thr	Gly	Val	Thr	Thr	Gln	Gly	Val	Lys	Ser	Leu		
				1365					1370					1375			
ctt	acc	agc	atg	tat	gtg	aag	gag	ttc	ctc	atc	tcc	agc	agt	caa	gat	4176	
Leu	Thr	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Ile	Ser	Ser	Ser	Gln	Asp		
			1380					1385						1390			
ggc	cat	cag	tgg	act	ctc	ttt	ttt	cag	aat	ggc	aaa	gta	aag	gtt	ttt	4224	
Gly	His	Gln	Trp	Thr	Leu	Phe	Phe	Gln	Asn	Gly	Lys	Val	Lys	Val	Phe		
		1395					1400					1405					
cag	gga	aat	caa	gac	tcc	ttc	aca	cct	gtg	gtg	aac	tct	cta	gac	cca	4272	
Gln	Gly	Asn	Gln	Asp	Ser	Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro		
	1410					1415					1420						
ccg	tta	ctg	act	cgc	tac	ctt	cga	att	cac	ccc	cag	agt	tgg	gtg	cac	4320	
Pro	Leu	Leu	Thr	Arg	Tyr	Leu	Arg	Ile	His	Pro	Gln	Ser	Trp	Val	His		
1425					1430					1435					1440		

cag att gcc ctg agg atg gag gtt ctg ggc tgc gag gca cag gac ctc 4368
 Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu
 1445 1450 1455

tac 4371
 Tyr

<210> 17
 <211> 1457
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> HP46/SQ-- factor VIII having the following
 domains: Alp-A2h-aph-A3h-Clh-C2h

<400> 17
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
 1 5 10 15
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
 245 250 255
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
 260 265 270
 Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
 275 280 285
 Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
 290 295 300
 Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
 305 310 315 320
 Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
 325 330 335
 His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
 340 345 350
 Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn
 355 360 365

Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
370						375					380				
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385						390				395					400
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
				405					410						415
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
			420					425					430		
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met
		435					440					445			
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470					475					480
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
				485					490						495
His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
			500					505					510		
Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe
		515					520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg
545					550					555					560
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
				565				570							575
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
			580					585					590		
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu
		595					600					605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp
	610					615					620				
Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
625					630					635					640
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
				645				650						655	
Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
			660					665					670		
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
	675						680					685			
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro
	690					695					700				
Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly
705					710					715					720
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp
				725					730					735	
Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys
			740					745					750		
Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Pro	Pro	Val	Leu
		755					760					765			
Lys	Arg	His	Gln	Arg	Glu	Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln
	770					775					780				
Glu	Glu	Ile	Asp	Tyr	Asp	Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu
785					790					795					800
Asp	Phe	Asp	Ile	Tyr	Asp	Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe
				805					810					815	
Gln	Lys	Lys	Thr	Arg	His	Tyr	Phe	Ile	Ala	Ala	Val	Glu	Arg	Leu	Trp
			820					825					830		
Asp	Tyr	Gly	Met	Ser	Ser	Ser	Pro	His	Val	Leu	Arg	Asn	Arg	Ala	Gln
		835					840					845			
Ser	Gly	Ser	Val	Pro	Gln	Phe	Lys	Lys	Val	Val	Phe	Gln	Glu	Phe	Thr
	850					855					860				
Asp	Gly	Ser	Phe	Thr	Gln	Pro	Leu	Tyr	Arg	Gly	Glu	Leu	Asn	Glu	His
865					870					875					880
Leu	Gly	Leu	Leu	Gly	Pro	Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile
				885					890						895

Met	Val	Thr	Phe	Arg	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	
			900					905					910			
Ser	Leu	Ile	Ser	Tyr	Glu	Glu	Asp	Gln	Arg	Gln	Gly	Ala	Glu	Pro	Arg	
		915					920					925				
Lys	Asn	Phe	Val	Lys	Pro	Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val	
	930					935					940					
Gln	His	His	Met	Ala	Pro	Thr	Lys	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	
945					950					955					960	
Ala	Tyr	Phe	Ser	Asp	Val	Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	
				965					970					975		
Ile	Gly	Pro	Leu	Leu	Val	Cys	His	Thr	Asn	Thr	Leu	Asn	Pro	Ala	His	
			980					985					990			
Gly	Arg	Gln	Val	Thr	Val	Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	
	995						1000					1005				
Asp	Glu	Thr	Lys	Ser	Trp	Tyr	Phe	Thr	Glu	Asn	Met	Glu	Arg	Asn	Cys	
	1010					1015					1020					
Arg	Ala	Pro	Cys	Asn	Ile	Gln	Met	Glu	Asp	Pro	Thr	Phe	Lys	Glu	Asn	
1025					1030					1035					1040	
Tyr	Arg	Phe	His	Ala	Ile	Asn	Gly	Tyr	Ile	Met	Asp	Thr	Leu	Pro	Gly	
				1045					1050					1055		
Leu	Val	Met	Ala	Gln	Asp	Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	
			1060					1065					1070			
Gly	Ser	Asn	Glu	Asn	Ile	His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	
	1075						1080					1085				
Thr	Val	Arg	Lys	Lys	Glu	Glu	Tyr	Lys	Met	Ala	Leu	Tyr	Asn	Leu	Tyr	
	1090					1095					1100					
Pro	Gly	Val	Phe	Glu	Thr	Val	Glu	Met	Leu	Pro	Ser	Lys	Ala	Gly	Ile	
1105					1110					1115					1120	
Trp	Arg	Val	Glu	Cys	Leu	Ile	Gly	Glu	His	Leu	His	Ala	Gly	Met	Ser	
				1125					1130					1135		
Thr	Leu	Phe	Leu	Val	Tyr	Ser	Asn	Lys	Cys	Gln	Thr	Pro	Leu	Gly	Met	
			1140					1145					1150			
Ala	Ser	Gly	His	Ile	Arg	Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	Gln	Tyr	
	1155						1160					1165				
Gly	Gln	Trp	Ala	Pro	Lys	Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	
	1170					1175					1180					
Asn	Ala	Trp	Ser	Thr	Lys	Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	
1185					1190					1195					1200	
Leu	Ala	Pro	Met	Ile	Ile	His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	
				1205					1210					1215		
Lys	Phe	Ser	Ser	Leu	Tyr	Ile	Ser	Gln	Phe	Ile	Ile	Met	Tyr	Ser	Leu	
			1220					1225					1230			
Asp	Gly	Lys	Lys	Trp	Gln	Thr	Tyr	Arg	Gly	Asn	Ser	Thr	Gly	Thr	Leu	
	1235						1240					1245				
Met	Val	Phe	Phe	Gly	Asn	Val	Asp	Ser	Ser	Gly	Ile	Lys	His	Asn	Ile	
	1250					1255					1260					
Phe	Asn	Pro	Pro	Ile	Ile	Ala	Arg	Tyr	Ile	Arg	Leu	His	Pro	Thr	His	
1265					1270					1275					1280	
Tyr	Ser	Ile	Arg	Ser	Thr	Leu	Arg	Met	Glu	Leu	Met	Gly	Cys	Asp	Leu	
				1285					1290					1295		
Asn	Ser	Cys	Ser	Met	Pro	Leu	Gly	Met	Glu	Ser	Lys	Ala	Ile	Ser	Asp	
			1300					1305					1310			
Ala	Gln	Ile	Thr	Ala	Ser	Ser	Tyr	Phe	Thr	Asn	Met	Phe	Ala	Thr	Trp	
	1315						1320					1325				
Ser	Pro	Ser	Lys	Ala	Arg	Leu	His	Leu	Gln	Gly	Arg	Ser	Asn	Ala	Trp	
	1330					1335					1340					
Arg	Pro	Gln	Val	Asn	Asn	Pro	Lys	Glu	Trp	Leu	Gln	Val	Asp	Phe	Gln	
1345					1350					1355					1360	
Lys	Thr	Met	Lys	Val	Thr	Gly	Val	Thr	Thr	Gln	Gly	Val	Lys	Ser	Leu	
				1365					1370					1375		
Leu	Thr	Ser	Met	Tyr	Val	Lys	Glu	Phe	Leu	Ile	Ser	Ser	Ser	Gln	Asp	
			1380					1385					1390			
Gly	His	Gln	Trp	Thr	Leu	Phe	Phe	Gln	Asn	Gly	Lys	Val	Lys	Val	Phe	
	1395						1400					1405				
Gln	Gly	Asn	Gln	Asp	Ser	Phe	Thr	Pro	Val	Val	Asn	Ser	Leu	Asp	Pro	
	1410					1415						1420				

Pro Leu Leu Thr Arg Tyr Leu Arg Ile His Pro Gln Ser Trp Val His
 1425 1430 1435 1440
 Gln Ile Ala Leu Arg Met Glu Val Leu Gly Cys Glu Ala Gln Asp Leu
 1445 1450 1455
 Tyr

<210> 18
 <211> 4401
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> hybrid human and porcine factor VIII sequence

<221> CDS
 <222> (1)...(4401)
 <223> HP47/OL -- factor VIII having the following
 domains: Alp-A2h-app-A3p-C1h-C2h

<400> 18
 atg cag cta gag ctc tcc acc tgt gtc ttt ctg tgt ctc ttg cca ctc 48
 Met Gln Leu Glu Leu Ser Thr Cys Val Phe Leu Cys Leu Leu Pro Leu
 1 5 10 15
 ggc ttt agt gcc atc agg aga tac tac ctg ggc gca gtg gaa ctg tcc 96
 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
 Trp Asp Tyr Arg Gln Ser Glu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 aga ttt cct gct aca gcg cca gga gct ctt ccg ttg ggc ccg tca gtc 192
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 ctg tac aaa aag act gtg ttc gta gag ttc acg gat caa ctt ttc agc 240
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 gtt gcc agg ccc agg cca cca tgg atg ggt ctg ctg ggt cct acc atc 288
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
 Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 tct cat ccc gtt agt ctt cac gct gtc ggc gtc tcc ttc tgg aaa tct 384
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 tcc gaa ggc gct gaa tat gag gat cac acc agc caa agg gag aag gaa 432
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 gac gat aaa gtc ctt ccc ggt aaa agc caa acc tac gtc tgg cag gtc 480
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 ctg aaa gaa aat ggt cca aca gcc tct gac cca cca tgt ctt acc tac 528
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175

tca tac ctg tct cac gtg gac ctg gtg aaa gac ctg aat tcg ggc ctc	576
Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu	
180 185 190	
att gga gcc ctg ctg gtt tgt aga gaa ggg agt ctg acc aga gaa agg	624
Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg	
195 200 205	
acc cag aac ctg cac gaa ttt gta cta ctt ttt gct gtc ttt gat gaa	672
Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu	
210 215 220	
ggg aaa agt tgg cac tca gca aga aat gac tcc tgg aca cgg gcc atg	720
Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met	
225 230 235 240	
gat ccc gca cct gcc agg gcc cag cct gca atg cac aca gtc aat ggc	768
Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly	
245 250 255	
tat gtc aac agg tct ctg cca ggt ctg atc gga tgt cat aag aaa tca	816
Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser	
260 265 270	
gtc tac tgg cac gtg att gga atg ggc acc agc ccg gaa gtg cac tcc	864
Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser	
275 280 285	
att ttt ctt gaa ggc cac acg ttt ctc gtg agg cac cat cgc cag gct	912
Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala	
290 295 300	
tcc ttg gag atc tcg cca cta act ttc ctc act gct cag aca ttc ctg	960
Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu	
305 310 315 320	
atg gac ctt ggc cag ttc cta ctg ttt tgt cat atc tct tcc cac cac	1008
Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His	
325 330 335	
cat ggt ggc atg gag gct cac gtc aga gta gaa agc tgc gcc gag gag	1056
His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu	
340 345 350	
ccc cag ctg cgg agg aaa gct gat gaa gag gaa gat tat gat gac aat	1104
Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn	
355 360 365	
ttg tac gac tcg gac atg gac gtg gtc cgg ctc gat ggt gac gac gtg	1152
Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val	
370 375 380	
tct ccc ttt atc caa atc cgc tca gtt gcc aag aag cat cct aaa act	1200
Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr	
385 390 395 400	
tgg gta cat tac att gct gct gaa gag gag gac tgg gac tat gct ccc	1248
Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro	
405 410 415	
tta gtc ctc gcc ccc gat gac aga agt tat aaa agt caa tat ttg aac	1296
Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn	
420 425 430	
aat ggc cct cag cgg att ggt agg aag tac aaa aaa gtc cga ttt atg	1344
Asn Gly Pro Gln Arg Ile Gly Arg Lys Lys Lys Val Arg Phe Met	

435	440	445	
gca tac aca gat gaa acc ttt aag acg cgt gaa gct att cag cat gaa Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu 450 455 460			1392
tca gga atc ttg gga cct tta ctt tat ggg gaa gtt gga gac aca ctg Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu 465 470 475 480			1440
ttg att ata ttt aag aat caa gca agc aga cca tat aac atc tac cct Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro 485 490 495			1488
cac gga atc act gat gtc cgt cct ttg tat tca agg aga tta cca aaa His Gly Ile Thr Asp Val Arg Pro Leu Tyr Ser Arg Arg Leu Pro Lys 500 505 510			1536
ggg gta aaa cat ttg aag gat ttt cca att ctg cca gga gaa ata ttc Gly Val Lys His Leu Lys Asp Phe Pro Ile Leu Pro Gly Glu Ile Phe 515 520 525			1584
aaa tat aaa tgg aca gtg act gta gaa gat ggg cca act aaa tca gat Lys Tyr Lys Trp Thr Val Thr Val Glu Asp Gly Pro Thr Lys Ser Asp 530 535 540			1632
ccg cgg tgc ctg acc cgc tat tac tct agt ttc gtt aat atg gag aga Pro Arg Cys Leu Thr Arg Tyr Tyr Ser Ser Phe Val Asn Met Glu Arg 545 550 555 560			1680
gat cta gct tca gga ctc att ggc cct ctc ctc atc tgc tac aaa gaa Asp Leu Ala Ser Gly Leu Ile Gly Pro Leu Leu Ile Cys Tyr Lys Glu 565 570 575			1728
tct gta gat caa aga gga aac cag ata atg tca gac aag agg aat gtc Ser Val Asp Gln Arg Gly Asn Gln Ile Met Ser Asp Lys Arg Asn Val 580 585 590			1776
atc ctg ttt tct gta ttt gat gag aac cga agc tgg tac ctc aca gag Ile Leu Phe Ser Val Phe Asp Glu Asn Arg Ser Trp Tyr Leu Thr Glu 595 600 605			1824
aat ata caa cgc ttt ctc ccc aat cca gct gga gtg cag ctt gag gat Asn Ile Gln Arg Phe Leu Pro Asn Pro Ala Gly Val Gln Leu Glu Asp 610 615 620			1872
cca gag ttc caa gcc tcc aac atc atg cac agc atc aat ggc tat gtt Pro Glu Phe Gln Ala Ser Asn Ile Met His Ser Ile Asn Gly Tyr Val 625 630 635 640			1920
ttt gat agt ttg cag ttg tca gtt tgt ttg cat gag gtg gca tac tgg Phe Asp Ser Leu Gln Leu Ser Val Cys Leu His Glu Val Ala Tyr Trp 645 650 655			1968
tac att cta agc att gga gca cag act gac ttc ctt tct gtc ttc ttc Tyr Ile Leu Ser Ile Gly Ala Gln Thr Asp Phe Leu Ser Val Phe Phe 660 665 670			2016
tct gga tat acc ttc aaa cac aaa atg gtc tat gaa gac aca ctc acc Ser Gly Tyr Thr Phe Lys His Lys Met Val Tyr Glu Asp Thr Leu Thr 675 680 685			2064
cta ttc cca ttc tca gga gaa act gtc ttc atg tcg atg gaa aac cca Leu Phe Pro Phe Ser Gly Glu Thr Val Phe Met Ser Met Glu Asn Pro 690 695 700			2112

ggc cta tgg att ctg ggg tgc cac aac tca gac ttt cgg aac aga ggc	2160
Gly Leu Trp Ile Leu Gly Cys His Asn Ser Asp Phe Arg Asn Arg Gly	
705 710 715 720	
atg acc gcc tta ctg aag gtt tct agt tgt gac aag aac act ggt gat	2208
Met Thr Ala Leu Leu Lys Val Ser Ser Cys Asp Lys Asn Thr Gly Asp	
725 730 735	
tat tac gag gac agt tat gaa gat att tca gca tac ttg ctg agt aaa	2256
Tyr Tyr Glu Asp Ser Tyr Glu Asp Ile Ser Ala Tyr Leu Leu Ser Lys	
740 745 750	
aac aat gcc att gaa cct agg agc ttt gcc cag aat tca aga ccc cct	2304
Asn Asn Ala Ile Glu Pro Arg Ser Phe Ala Gln Asn Ser Arg Pro Pro	
755 760 765	
agt gcg agc gct cca aag cct ccg gtc ctg cga cgg cat cag agg gac	2352
Ser Ala Ser Ala Pro Lys Pro Pro Val Leu Arg Arg His Gln Arg Asp	
770 775 780	
ata agc ctt cct act ttt cag ccg gag gaa gac aaa atg gac tat gat	2400
Ile Ser Leu Pro Thr Phe Gln Pro Glu Glu Asp Lys Met Asp Tyr Asp	
785 790 795 800	
gat atc ttc tca act gaa acg aag gga gaa gat ttt gac att tac ggt	2448
Asp Ile Phe Ser Thr Glu Thr Lys Gly Glu Asp Phe Asp Ile Tyr Gly	
805 810 815	
gag gat gaa aat cag gac cct cgc agc ttt cag aag aga acc cga cac	2496
Glu Asp Glu Asn Gln Asp Pro Arg Ser Phe Gln Lys Arg Thr Arg His	
820 825 830	
tat ttc att gct gcg gtg gag cag ctc tgg gat tac ggg atg agc gaa	2544
Tyr Phe Ile Ala Ala Val Glu Gln Leu Trp Asp Tyr Gly Met Ser Glu	
835 840 845	
tcc ccc cgg gcg cta aga aac agg gct cag aac gga gag gtg cct cgg	2592
Ser Pro Arg Ala Leu Arg Asn Arg Ala Gln Asn Gly Glu Val Pro Arg	
850 855 860	
ttc aag aag gtg gtc ttc cgg gaa ttt gct gac ggc tcc ttc acg cag	2640
Phe Lys Lys Val Val Phe Arg Glu Phe Ala Asp Gly Ser Phe Thr Gln	
865 870 875 880	
ccg tcg tac cgc ggg gaa ctc aac aaa cac ttg ggg ctc ttg gga ccc	2688
Pro Ser Tyr Arg Gly Glu Leu Asn Lys His Leu Gly Leu Leu Gly Pro	
885 890 895	
tac atc aga gcg gaa gtt gaa gac aac atc atg gta act ttc aaa aac	2736
Tyr Ile Arg Ala Glu Val Glu Asp Asn Ile Met Val Thr Phe Lys Asn	
900 905 910	
cag gcg tct cgt ccc tat tcc ttc tac tcg agc ctt att tct tat ccg	2784
Gln Ala Ser Arg Pro Tyr Ser Phe Tyr Ser Ser Leu Ile Ser Tyr Pro	
915 920 925	
gat gat cag gag caa ggg gca gaa cct cga cac aac ttc gtc cag cca	2832
Asp Asp Gln Glu Gln Gly Ala Glu Pro Arg His Asn Phe Val Gln Pro	
930 935 940	
aat gaa acc aga act tac ttt tgg aaa gtg cag cat cac atg gca ccc	2880
Asn Glu Thr Arg Thr Tyr Phe Trp Lys Val Gln His His Met Ala Pro	
945 950 955 960	
aca gaa gac gag ttt gac tgc aaa gcc tgg gcc tac ttt tct gat gtt	2928
Thr Glu Asp Glu Phe Asp Cys Lys Ala Trp Ala Tyr Phe Ser Asp Val	

965										970					975					
gac	ctg	gaa	aaa	gat	gtg	cac	tca	ggc	ttg	atc	ggc	ccc	ctt	ctg	atc	2976				
Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile					
			980				985						990							
tgc	cgc	gcc	aac	acc	ctg	aac	gct	gct	cac	ggg	aga	caa	gtg	acc	gtg	3024				
Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	Ala	His	Gly	Arg	Gln	Val	Thr	Val					
			995				1000						1005							
caa	gaa	ttt	gct	ctg	ttt	ttc	act	att	ttt	gat	gag	aca	aag	agc	tgg	3072				
Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp					
			1010				1015						1020							
tac	ttc	act	gaa	aat	gtg	gaa	agg	aac	tgc	cgg	gcc	ccc	tgc	cat	ctg	3120				
Tyr	Phe	Thr	Glu	Asn	Val	Glu	Arg	Asn	Cys	Arg	Ala	Pro	Cys	His	Leu					
			1025				1030						1040							
cag	atg	gag	gac	ccc	act	ctg	aaa	gaa	aac	tat	cgc	ttc	cat	gca	atc	3168				
Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile					
			1045							1050			1055							
aat	ggc	tat	gtg	atg	gat	aca	ctc	cct	ggc	tta	gta	atg	gct	cag	aat	3216				
Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	Met	Ala	Gln	Asn					
			1060							1065			1070							
caa	agg	atc	cga	tgg	tat	ctg	ctc	agc	atg	ggc	agc	aat	gaa	aat	atc	3264				
Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile					
			1075							1080			1085							
cat	tcg	att	cat	ttt	agc	gga	cac	gtg	ttc	agt	gta	cgg	aaa	aag	gag	3312				
His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Ser	Val	Arg	Lys	Lys	Glu					
			1090				1095						1100							
gag	tat	aaa	atg	gcc	gtg	tac	aat	ctc	tat	ccg	ggg	gtc	ttt	gag	aca	3360				
Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr					
			1105				1110						1120							
gtg	gaa	atg	cta	ccg	tcc	aaa	gtt	gga	att	tgg	cga	ata	gaa	tgc	ctg	3408				
Val	Glu	Met	Leu	Pro	Ser	Lys	Val	Gly	Ile	Trp	Arg	Ile	Glu	Cys	Leu					
			1125							1130			1135							
att	ggc	gag	cac	ctg	caa	gct	ggg	atg	agc	acg	act	ttc	ctg	gtg	tac	3456				
Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Thr	Phe	Leu	Val	Tyr					
			1140				1145						1150							
agc	aag	aag	tgt	cag	act	ccc	ctg	gga	atg	gct	tct	gga	cac	att	aga	3504				
Ser	Lys	Lys	Cys	Gln	Thr	Pro	Leu	Gly	Met	Ala	Ser	Gly	His	Ile	Arg					
			1155				1160						1165							
gat	ttt	cag	att	aca	gct	tca	gga	caa	tat	gga	cag	tgg	gcc	cca	aag	3552				
Asp	Phe	Gln	Ile	Thr	Ala	Ser	Gly	Gln	Tyr	Gly	Gln	Trp	Ala	Pro	Lys					
			1170				1175						1180							
ctg	gcc	aga	ctt	cat	tat	tcc	gga	tca	atc	aat	gcc	tgg	agc	acc	aag	3600				
Leu	Ala	Arg	Leu	His	Tyr	Ser	Gly	Ser	Ile	Asn	Ala	Trp	Ser	Thr	Lys					
			1185				1190						1200							
gag	ccc	ttt	tct	tgg	atc	aag	gtg	gat	ctg	ttg	gca	cca	atg	att	att	3648				
Glu	Pro	Phe	Ser	Trp	Ile	Lys	Val	Asp	Leu	Leu	Ala	Pro	Met	Ile	Ile					
			1205							1210			1215							
cac	ggc	atc	aag	acc	cag	ggg	gcc	cgt	cag	aag	ttc	tcc	agc	ctc	tac	3696				
His	Gly	Ile	Lys	Thr	Gln	Gly	Ala	Arg	Gln	Lys	Phe	Ser	Ser	Leu	Tyr					
			1220				1225						1230							

atc tct cag ttt atc atc atg tat agt ctt gat ggg aag aag tgg cag Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln 1235 1240 1245	3744
act tat cga gga aat tcc act gga acc tta atg gtc ttc ttt ggc aat Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn 1250 1255 1260	3792
gtg gat tca tct ggg ata aaa cac aat att ttt aac cct cca att att Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile 1265 1270 1275 1280	3840
gct cga tac atc cgt ttg cac cca act cat tat agc att cgc agc act Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr 1285 1290 1295	3888
ctt cgc atg gag ttg atg ggc tgt gat tta aat agt tgc agc atg cca Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro 1300 1305 1310	3936
ttg gga atg gag agt aaa gca ata tca gat gca cag att act gct tca Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser 1315 1320 1325	3984
tcc tac ttt acc aat atg ttt gcc acc tgg tct cct tca aaa gct cga Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg 1330 1335 1340	4032
ctt cac ctc caa ggg agg agt aat gcc tgg aga cct cag gtg aat aat Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn 1345 1350 1355 1360	4080
cca aaa gag tgg ctg caa gtg gac ttc cag aag aca atg aaa gtc aca Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr 1365 1370 1375	4128
gga gta act act cag gga gta aaa tct ctg ctt acc agc atg tat gtg Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val 1380 1385 1390	4176
aag gag ttc ctc atc tcc agc agt caa gat ggc cat cag tgg act ctc Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu 1395 1400 1405	4224
ttt ttt cag aat ggc aaa gta aag gtt ttt cag gga aat caa gac tcc Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser 1410 1415 1420	4272
ttc aca cct gtg gtg aac tct cta gac cca ccg tta ctg act cgc tac Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr 1425 1430 1435 1440	4320
ctt cga att cac ccc cag agt tgg gtg cac cag att gcc ctg agg atg Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met 1445 1450 1455	4368
gag gtt ctg ggc tgc gag gca cag gac ctc tac Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr 1460 1465	4401

<210> 19
 <211> 1467
 <212> PRT
 <213> Artificial Sequence

<220>.
 <223> HP47/OL -- factor VIII having the following
 domains: Alp-A2h-app-A3p-C1h-C2h

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 Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
 20 25 30
 Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
 35 40 45
 Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
 50 55 60
 Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
 65 70 75 80
 Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
 85 90 95
 Gln Ala Glu Val Tyr Asp Thr Val Val Val Thr Leu Lys Asn Met Ala
 100 105 110
 Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
 115 120 125
 Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
 130 135 140
 Asp Asp Lys Val Leu Pro Gly Lys Ser Gln Thr Tyr Val Trp Gln Val
 145 150 155 160
 Leu Lys Glu Asn Gly Pro Thr Ala Ser Asp Pro Pro Cys Leu Thr Tyr
 165 170 175
 Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
 180 185 190
 Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
 195 200 205
 Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
 210 215 220
 Gly Lys Ser Trp His Ser Ala Arg Asn Asp Ser Trp Thr Arg Ala Met
 225 230 235 240
 Asp Pro Ala Pro Ala Arg Ala Gln Pro Ala Met His Thr Val Asn Gly
 245 250 255
 Tyr Val Asn Arg Ser Leu Pro Gly Leu Ile Gly Cys His Lys Lys Ser
 260 265 270
 Val Tyr Trp His Val Ile Gly Met Gly Thr Ser Pro Glu Val His Ser
 275 280 285
 Ile Phe Leu Glu Gly His Thr Phe Leu Val Arg His His Arg Gln Ala
 290 295 300
 Ser Leu Glu Ile Ser Pro Leu Thr Phe Leu Thr Ala Gln Thr Phe Leu
 305 310 315 320
 Met Asp Leu Gly Gln Phe Leu Leu Phe Cys His Ile Ser Ser His His
 325 330 335
 His Gly Gly Met Glu Ala His Val Arg Val Glu Ser Cys Ala Glu Glu
 340 345 350
 Pro Gln Leu Arg Arg Lys Ala Asp Glu Glu Glu Asp Tyr Asp Asp Asn
 355 360 365
 Leu Tyr Asp Ser Asp Met Asp Val Val Arg Leu Asp Gly Asp Asp Val
 370 375 380
 Ser Pro Phe Ile Gln Ile Arg Ser Val Ala Lys Lys His Pro Lys Thr
 385 390 395 400
 Trp Val His Tyr Ile Ala Ala Glu Glu Glu Asp Trp Asp Tyr Ala Pro
 405 410 415
 Leu Val Leu Ala Pro Asp Asp Arg Ser Tyr Lys Ser Gln Tyr Leu Asn
 420 425 430
 Asn Gly Pro Gln Arg Ile Gly Arg Lys Tyr Lys Lys Val Arg Phe Met
 435 440 445
 Ala Tyr Thr Asp Glu Thr Phe Lys Thr Arg Glu Ala Ile Gln His Glu
 450 455 460
 Ser Gly Ile Leu Gly Pro Leu Leu Tyr Gly Glu Val Gly Asp Thr Leu
 465 470 475 480
 Leu Ile Ile Phe Lys Asn Gln Ala Ser Arg Pro Tyr Asn Ile Tyr Pro

77

1010		1015		1020
Tyr Phe Thr Glu Asn Val Glu Arg Asn Cys Arg Ala Pro Cys His Leu				
1025		1030		1035
Gln Met Glu Asp Pro Thr Leu Lys Glu Asn Tyr Arg Phe His Ala Ile				1040
	1045		1050	1055
Asn Gly Tyr Val Met Asp Thr Leu Pro Gly Leu Val Met Ala Gln Asn				
	1060		1065	1070
Gln Arg Ile Arg Trp Tyr Leu Leu Ser Met Gly Ser Asn Glu Asn Ile				
	1075		1080	1085
His Ser Ile His Phe Ser Gly His Val Phe Ser Val Arg Lys Lys Glu				
	1090		1095	1100
Glu Tyr Lys Met Ala Val Tyr Asn Leu Tyr Pro Gly Val Phe Glu Thr				
1105		1110		1115
Val Glu Met Leu Pro Ser Lys Val Gly Ile Trp Arg Ile Glu Cys Leu				1120
	1125		1130	1135
Ile Gly Glu His Leu Gln Ala Gly Met Ser Thr Thr Phe Leu Val Tyr				
	1140		1145	1150
Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg				
	1155		1160	1165
Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys				
	1170		1175	1180
Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys				
1185		1190		1195
Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile				1200
	1205		1210	1215
His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr				
	1220		1225	1230
Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln				
	1235		1240	1245
Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn				
	1250		1255	1260
Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile				
1265		1270		1275
Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr				
	1285		1290	1295
Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro				
	1300		1305	1310
Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser				
	1315		1320	1325
Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg				
	1330		1335	1340
Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn				
1345		1350		1355
Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr				
	1365		1370	1375
Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val				
	1380		1385	1390
Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu				
	1395		1400	1405
Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser				
	1410		1415	1420
Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr				
1425		1430		1435
Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met				
	1445		1450	1455
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<211> 4401

<212> DNA

<213> Artificial Sequence

<220>

<223> hybrid human and porcine factor VIII sequence

<221> CDS
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Gly Phe Ser Ala Ile Arg Arg Tyr Tyr Leu Gly Ala Val Glu Leu Ser
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tgg gac tac cgg caa agt gaa ctc ctc cgt gag ctg cac gtg gac acc 144
Trp Asp Tyr Arg Gln Ser Glu Leu Leu Arg Glu Leu His Val Asp Thr
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Arg Phe Pro Ala Thr Ala Pro Gly Ala Leu Pro Leu Gly Pro Ser Val
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Leu Tyr Lys Lys Thr Val Phe Val Glu Phe Thr Asp Gln Leu Phe Ser
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Val Ala Arg Pro Arg Pro Pro Trp Met Gly Leu Leu Gly Pro Thr Ile
85 90 95

cag gct gag gtt tac gac acg gtg gtc gtt acc ctg aag aac atg gct 336
Gln Ala Glu Val Tyr Asp Thr Val Val Thr Leu Lys Asn Met Ala
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Ser His Pro Val Ser Leu His Ala Val Gly Val Ser Phe Trp Lys Ser
115 120 125

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Ser Glu Gly Ala Glu Tyr Glu Asp His Thr Ser Gln Arg Glu Lys Glu
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Ser Tyr Leu Ser His Val Asp Leu Val Lys Asp Leu Asn Ser Gly Leu
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Ile Gly Ala Leu Leu Val Cys Arg Glu Gly Ser Leu Thr Arg Glu Arg
195 200 205

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Thr Gln Asn Leu His Glu Phe Val Leu Leu Phe Ala Val Phe Asp Glu
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225 230 235 240

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Gly	Lys	Ser	Trp	His	Ser	Ala	Arg	Asn	Asp	Ser	Trp	Thr	Arg	Ala	Met
225					230				235						240
Asp	Pro	Ala	Pro	Ala	Arg	Ala	Gln	Pro	Ala	Met	His	Thr	Val	Asn	Gly
				245					250					255	
Tyr	Val	Asn	Arg	Ser	Leu	Pro	Gly	Leu	Ile	Gly	Cys	His	Lys	Lys	Ser
			260					265					270		
Val	Tyr	Trp	His	Val	Ile	Gly	Met	Gly	Thr	Ser	Pro	Glu	Val	His	Ser
	275					280						285			
Ile	Phe	Leu	Glu	Gly	His	Thr	Phe	Leu	Val	Arg	His	His	Arg	Gln	Ala
	290					295					300				
Ser	Leu	Glu	Ile	Ser	Pro	Leu	Thr	Phe	Leu	Thr	Ala	Gln	Thr	Phe	Leu
305					310				315						320
Met	Asp	Leu	Gly	Gln	Phe	Leu	Leu	Phe	Cys	His	Ile	Ser	Ser	His	His
			325						330					335	
His	Gly	Gly	Met	Glu	Ala	His	Val	Arg	Val	Glu	Ser	Cys	Ala	Glu	Glu
			340					345					350		
Pro	Gln	Leu	Arg	Arg	Lys	Ala	Asp	Glu	Glu	Glu	Asp	Tyr	Asp	Asp	Asn
	355					360						365			
Leu	Tyr	Asp	Ser	Asp	Met	Asp	Val	Val	Arg	Leu	Asp	Gly	Asp	Asp	Val
	370				375						380				
Ser	Pro	Phe	Ile	Gln	Ile	Arg	Ser	Val	Ala	Lys	Lys	His	Pro	Lys	Thr
385					390				395						400
Trp	Val	His	Tyr	Ile	Ala	Ala	Glu	Glu	Glu	Asp	Trp	Asp	Tyr	Ala	Pro
			405					410						415	
Leu	Val	Leu	Ala	Pro	Asp	Asp	Arg	Ser	Tyr	Lys	Ser	Gln	Tyr	Leu	Asn
			420					425					430		
Asn	Gly	Pro	Gln	Arg	Ile	Gly	Arg	Lys	Tyr	Lys	Lys	Val	Arg	Phe	Met
	435					440						445			
Ala	Tyr	Thr	Asp	Glu	Thr	Phe	Lys	Thr	Arg	Glu	Ala	Ile	Gln	His	Glu
	450					455					460				
Ser	Gly	Ile	Leu	Gly	Pro	Leu	Leu	Tyr	Gly	Glu	Val	Gly	Asp	Thr	Leu
465					470				475						480
Leu	Ile	Ile	Phe	Lys	Asn	Gln	Ala	Ser	Arg	Pro	Tyr	Asn	Ile	Tyr	Pro
			485						490					495	
His	Gly	Ile	Thr	Asp	Val	Arg	Pro	Leu	Tyr	Ser	Arg	Arg	Leu	Pro	Lys
			500					505					510		
Gly	Val	Lys	His	Leu	Lys	Asp	Phe	Pro	Ile	Leu	Pro	Gly	Glu	Ile	Phe
	515						520					525			
Lys	Tyr	Lys	Trp	Thr	Val	Thr	Val	Glu	Asp	Gly	Pro	Thr	Lys	Ser	Asp
	530					535					540				
Pro	Arg	Cys	Leu	Thr	Arg	Tyr	Tyr	Ser	Ser	Phe	Val	Asn	Met	Glu	Arg
545					550				555						560
Asp	Leu	Ala	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile	Cys	Tyr	Lys	Glu
			565					570						575	
Ser	Val	Asp	Gln	Arg	Gly	Asn	Gln	Ile	Met	Ser	Asp	Lys	Arg	Asn	Val
			580					585					590		
Ile	Leu	Phe	Ser	Val	Phe	Asp	Glu	Asn	Arg	Ser	Trp	Tyr	Leu	Thr	Glu
	595						600					605			
Asn	Ile	Gln	Arg	Phe	Leu	Pro	Asn	Pro	Ala	Gly	Val	Gln	Leu	Glu	Asp
	610					615					620				

Pro	Glu	Phe	Gln	Ala	Ser	Asn	Ile	Met	His	Ser	Ile	Asn	Gly	Tyr	Val
625					630				635						640
Phe	Asp	Ser	Leu	Gln	Leu	Ser	Val	Cys	Leu	His	Glu	Val	Ala	Tyr	Trp
			645					650						655	
Tyr	Ile	Leu	Ser	Ile	Gly	Ala	Gln	Thr	Asp	Phe	Leu	Ser	Val	Phe	Phe
			660					665					670		
Ser	Gly	Tyr	Thr	Phe	Lys	His	Lys	Met	Val	Tyr	Glu	Asp	Thr	Leu	Thr
		675					680					685			
Leu	Phe	Pro	Phe	Ser	Gly	Glu	Thr	Val	Phe	Met	Ser	Met	Glu	Asn	Pro
		690				695					700				
Gly	Leu	Trp	Ile	Leu	Gly	Cys	His	Asn	Ser	Asp	Phe	Arg	Asn	Arg	Gly
705					710					715					720
Met	Thr	Ala	Leu	Leu	Lys	Val	Ser	Ser	Cys	Asp	Lys	Asn	Thr	Gly	Asp
			725						730					735	
Tyr	Tyr	Glu	Asp	Ser	Tyr	Glu	Asp	Ile	Ser	Ala	Tyr	Leu	Leu	Ser	Lys
			740					745					750		
Asn	Asn	Ala	Ile	Glu	Pro	Arg	Ser	Phe	Ser	Gln	Asn	Ser	Arg	His	Pro
		755					760					765			
Ser	Thr	Arg	Ser	Gln	Asn	Pro	Pro	Val	Leu	Lys	Arg	His	Gln	Arg	Glu
		770				775					780				
Ile	Thr	Arg	Thr	Thr	Leu	Gln	Ser	Asp	Gln	Glu	Ile	Asp	Tyr	Asp	
785					790					795					800
Asp	Thr	Ile	Ser	Val	Glu	Met	Lys	Lys	Glu	Asp	Phe	Asp	Ile	Tyr	Asp
			805						810					815	
Glu	Asp	Glu	Asn	Gln	Ser	Pro	Arg	Ser	Phe	Gln	Lys	Arg	Thr	Arg	His
			820					825					830		
Tyr	Phe	Ile	Ala	Ala	Val	Glu	Gln	Leu	Trp	Asp	Tyr	Gly	Met	Ser	Glu
		835					840					845			
Ser	Pro	Arg	Ala	Leu	Arg	Asn	Arg	Ala	Gln	Asn	Gly	Glu	Val	Pro	Arg
		850				855					860				
Phe	Lys	Lys	Val	Val	Phe	Arg	Glu	Phe	Ala	Asp	Gly	Ser	Phe	Thr	Gln
865					870				875						880
Pro	Ser	Tyr	Arg	Gly	Glu	Leu	Asn	Lys	His	Leu	Gly	Leu	Leu	Gly	Pro
			885						890					895	
Tyr	Ile	Arg	Ala	Glu	Val	Glu	Asp	Asn	Ile	Met	Val	Thr	Phe	Lys	Asn
			900					905					910		
Gln	Ala	Ser	Arg	Pro	Tyr	Ser	Phe	Tyr	Ser	Ser	Leu	Ile	Ser	Tyr	Pro
		915					920					925			
Asp	Asp	Gln	Glu	Gln	Gly	Ala	Glu	Pro	Arg	Lys	Asn	Phe	Val	Lys	Pro
		930				935					940				
Asn	Glu	Thr	Lys	Thr	Tyr	Phe	Trp	Lys	Val	Gln	His	His	Met	Ala	Pro
945					950					955					960
Thr	Glu	Asp	Glu	Phe	Asp	Cys	Lys	Ala	Trp	Ala	Tyr	Phe	Ser	Asp	Val
			965						970					975	
Asp	Leu	Glu	Lys	Asp	Val	His	Ser	Gly	Leu	Ile	Gly	Pro	Leu	Leu	Ile
			980					985					990		
Cys	Arg	Ala	Asn	Thr	Leu	Asn	Ala	His	Gly	Arg	Gln	Val	Thr	Val	
		995					1000					1005			
Gln	Glu	Phe	Ala	Leu	Phe	Phe	Thr	Ile	Phe	Asp	Glu	Thr	Lys	Ser	Trp
		1010				1015						1020			
Tyr	Phe	Thr	Glu	Asn	Val	Glu	Arg	Asn	Cys	Arg	Ala	Pro	Cys	His	Leu
1025					1030					1035					1040
Gln	Met	Glu	Asp	Pro	Thr	Leu	Lys	Glu	Asn	Tyr	Arg	Phe	His	Ala	Ile
			1045						1050					1055	
Asn	Gly	Tyr	Val	Met	Asp	Thr	Leu	Pro	Gly	Leu	Val	Met	Ala	Gln	Asn
			1060					1065					1070		
Gln	Arg	Ile	Arg	Trp	Tyr	Leu	Leu	Ser	Met	Gly	Ser	Asn	Glu	Asn	Ile
		1075					1080					1085			
His	Ser	Ile	His	Phe	Ser	Gly	His	Val	Phe	Ser	Val	Arg	Lys	Lys	Glu
		1090				1095						1100			
Glu	Tyr	Lys	Met	Ala	Val	Tyr	Asn	Leu	Tyr	Pro	Gly	Val	Phe	Glu	Thr
1105					1110					1115					1120
Val	Glu	Met	Leu	Pro	Ser	Lys	Val	Gly	Ile	Trp	Arg	Asn	Arg	Cys	Leu
			1125						1130					1135	
Ile	Gly	Glu	His	Leu	Gln	Ala	Gly	Met	Ser	Thr	Thr	Phe	Leu	Val	Tyr
			1140					1145					1150		

Ser Lys Lys Cys Gln Thr Pro Leu Gly Met Ala Ser Gly His Ile Arg
 1155 1160 1165
 Asp Phe Gln Ile Thr Ala Ser Gly Gln Tyr Gly Gln Trp Ala Pro Lys
 1170 1175 1180
 Leu Ala Arg Leu His Tyr Ser Gly Ser Ile Asn Ala Trp Ser Thr Lys
 1185 1190 1195 1200
 Glu Pro Phe Ser Trp Ile Lys Val Asp Leu Leu Ala Pro Met Ile Ile
 1205 1210 1215
 His Gly Ile Lys Thr Gln Gly Ala Arg Gln Lys Phe Ser Ser Leu Tyr
 1220 1225 1230
 Ile Ser Gln Phe Ile Ile Met Tyr Ser Leu Asp Gly Lys Lys Trp Gln
 1235 1240 1245
 Thr Tyr Arg Gly Asn Ser Thr Gly Thr Leu Met Val Phe Phe Gly Asn
 1250 1255 1260
 Val Asp Ser Ser Gly Ile Lys His Asn Ile Phe Asn Pro Pro Ile Ile
 1265 1270 1275 1280
 Ala Arg Tyr Ile Arg Leu His Pro Thr His Tyr Ser Ile Arg Ser Thr
 1285 1290 1295
 Leu Arg Met Glu Leu Met Gly Cys Asp Leu Asn Ser Cys Ser Met Pro
 1300 1305 1310
 Leu Gly Met Glu Ser Lys Ala Ile Ser Asp Ala Gln Ile Thr Ala Ser
 1315 1320 1325
 Ser Tyr Phe Thr Asn Met Phe Ala Thr Trp Ser Pro Ser Lys Ala Arg
 1330 1335 1340
 Leu His Leu Gln Gly Arg Ser Asn Ala Trp Arg Pro Gln Val Asn Asn
 1345 1350 1355 1360
 Pro Lys Glu Trp Leu Gln Val Asp Phe Gln Lys Thr Met Lys Val Thr
 1365 1370 1375
 Gly Val Thr Thr Gln Gly Val Lys Ser Leu Leu Thr Ser Met Tyr Val
 1380 1385 1390
 Lys Glu Phe Leu Ile Ser Ser Ser Gln Asp Gly His Gln Trp Thr Leu
 1395 1400 1405
 Phe Phe Gln Asn Gly Lys Val Lys Val Phe Gln Gly Asn Gln Asp Ser
 1410 1415 1420
 Phe Thr Pro Val Val Asn Ser Leu Asp Pro Pro Leu Leu Thr Arg Tyr
 1425 1430 1435 1440
 Leu Arg Ile His Pro Gln Ser Trp Val His Gln Ile Ala Leu Arg Met
 1445 1450 1455
 Glu Val Leu Gly Cys Glu Ala Gln Asp Leu Tyr
 1460 1465